

Review

Biological activities and distribution of plant saponins

S.G. Sparg, M.E. Light, J. van Staden*

Research Centre for Plant Growth and Development, University of KwaZulu-Natal, Pietermaritzburg, Private Bag X01, Scottsville 3209, South Africa

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Abstract

Plant saponins are widely distributed amongst plants and have a wide range of biological properties. The more recent investigations and findings into their biological activities were summarized. Isolation studies of saponins were examined to determine which are the more commonly studied plant families and in which families saponins have been identified.

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1. Introduction

Saponins are a vast group of glycosides, widely distributed in higher plants. Their surface-active properties are what distinguish these compounds from other glycosides. They dissolve in water to form colloidal solutions that foam upon shaking (Tyler et al., 1981). Saponin containing plants are sought after for use in household detergents (*sapo, onis* = soap) (Bruneton, 1995). One such example is the soapwort (*Saponaria officinalis* L.), which has been widely used for centuries. Saponins have also been sought after in the pharmaceutical industry because some form the starting point for the semi-synthesis of steroidal drugs. Many have pharmacological properties and are used in phytotherapy and in the cosmetic industry. They are believed to form the main constituents of many plant drugs and folk medicines, and are considered responsible for numerous pharmacological properties (Estrada et al., 2000). Liu and Henkel (2002) consider saponins and polyphenols key ingredients in traditional Chinese medicines, and are responsible for most of the observed biological effects. For example, the ginseng root (*Panax ginseng* C.A.Meyer, Araliaceae) is one of the

most important traditional oriental medicines and is now used worldwide (Fukuda et al., 2000). Saponins are said to make up the active major constituents of ginseng. The genus *Bupleurum* is officially listed in Chinese and Japanese Pharmacopoeias are used in Asian traditional medicines to treat different ailments. The dry roots of *Bupleurum frutescens* L. (Apiaceae) are traditionally used to treat disorders associated with inflammation. The main anti-inflammatory compounds found in *Bupleurum frutescens* are saikosaponins (Just et al., 1998). Active constituents of *Allium chinense* G.Don and *Allium macrostemon* Bunge (Alliaceae) the main sources of a Chinese Traditional medicine “Xiebai” which used as a treatment for chest pain, stenocardia and cardiac asthma have been shown to be saponins (Baba et al., 2000).

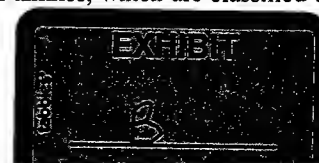
Most saponins have haemolytic properties and are toxic to most cold-blooded animals. The seeds of *Barringtonia asiatica* Kurz (Lecythidaceae) which have known to contain saponins, have been used traditionally by native Asian and Pacific fisherman for centuries to enhance their catches (Herlt et al., 2002). However, since these properties are not common to all saponins, they cannot be distinguished from other compounds on the basis of these properties alone (Bruneton, 1995).

Saponins can be classified into two groups based on the nature of their aglycone skeleton. The first group consists of the steroidal saponins, which are almost exclusively present in the monocotyledonous angiosperms. The second group consists of the triterpenoid saponins, which are the most common and occur mainly in the dicotyledonous angiosperms (Bruneton, 1995). Some authors distinguish a third group called steroidal amines, which are classified by

Abbreviations: CDDP, cisplatin; ED₅₀, median effective dose; HD₅₀, haemolytic dose of 50%; HD₁₀₀, haemolytic dose of 100%; HGF, human gingival fibroblasts; HIV, human immunodeficiency virus; HSC, human oral squamous cell carcinoma; HSV, anti-herpes simplex virus; IC₅₀, median inhibitory concentration; LC₅₀, median lethal concentration; LD₅₀, median lethal dose; LD₉₀, lethal dose at 90%; LD₉₅, lethal dose at 95%; MIC, minimum inhibitory concentration; TGF, transforming growth factor

* Corresponding author. Tel.: +27 33 260 5130; fax: +27 33 260 5897.

E-mail address: vanstadenj@ukzn.ac.za (J. van Staden).



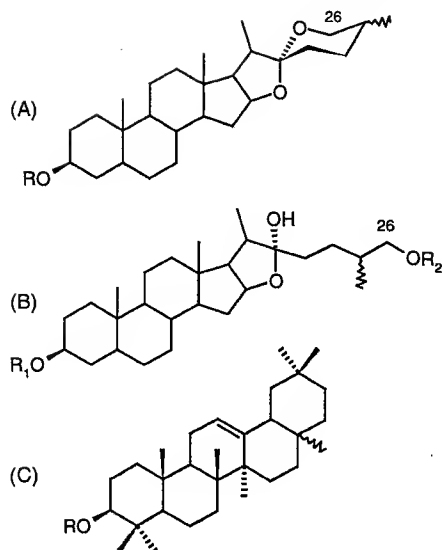


Fig. 1. Aglycone skeletons of (A) steroidal spirostane, (B) steroidal furostane, and (C) triterpenoid saponins. R = sugar moiety.

others as steroidal alkaloids (Bruneton, 1995). For the purpose of this review, only steroidal and triterpenoid saponins were considered. Steroidal saponins consist of a steroidal aglycone, a C₂₇ spirostane skeleton, generally comprising of a six-ring structure (Fig. 1A). In some cases, in fresh plant material, the hydroxyl group in the 26-position is engaged in a glycosidic linkage, and so the aglycone structure remains pentacyclic. This is referred to as a furostane skeleton (Fig. 1B). Triterpenoid saponins consist of a triterpenoid aglycone, which consists of a C₃₀ skeleton, comprising of a pentacyclic structure (Fig. 1C). According to Haralampidis et al. (2002), very little is known about the enzymes and biochemical pathways involved in saponin biosynthesis in plants. Haralampidis et al. (2002) review the biosynthesis of triterpenoid saponins and addressed recent advances in two key areas of saponin biosynthesis, namely the glycosylation of sapogenins and the cyclisation of 2,3-oxidosqualene.

Biological and pharmacological activities of saponins have been reported in several reviews with the most recent being Lacaille-Dubois and Wagner (1996). Similarly, this review will also summarize some of the important reports of biological active plant saponins of recent years (1998–2003) and will discuss the taxonomic distribution of recently isolated saponins.

2. Biological and pharmacological properties of saponins

2.1. Haemolytic activity

Saponins have the ability to rupture erythrocytes. This has lead to the development of the haemolytic assays for detecting the presence of saponins in drugs or plant extracts. The

haemolytic properties are generally attributed to the interaction between the saponins and the sterols of the erythrocyte membrane. As a result, the membrane bursts, causing an increase in permeability and a loss of haemoglobin. Baumann et al. (2000) investigated the effect of saponins on the membrane structure through haemolysis of human erythrocytes. The findings showed that saponin-lysed erythrocytes do not reseal, and therefore indicates that saponin damage to the lipid bilayer is irreversible.

Oda et al. (2000) reported on the haemolytic activity of 47 different plant derived saponins, purified from food and medicinal plants. It has been suggested that there is a relationship between the adjuvant and haemolytic activity of saponins, however, the results indicated that the adjuvant activity does not relate with haemolytic activity. A substance or compound is said to have adjuvant activity if when used with another active compound, it enhances the activity of the active compound. The level of haemolytic activity was attributed to the type of aglycone and the presence of sugar side chains. Saponins with an acyl residue or oxide-ring moiety tended to show haemolytic activity, except for lablaboside D, which did not show haemolytic activity despite possessing a acyl residue. Escin saponins found in *Aesculus hippocastanum* L. (Hippocastanaceae) and jujuboside saponins from *Zizyphus jujuba* Mill. (Rhamnaceae) had strong haemolytic activity.

Sindambiwe et al. (1998) tested a mixture of saponins isolated from *Maesa lanceolata* Forssk. (Myrsinaceae) for haemolytic activity. The maesasaponin mixture, showed very high haemolytic activity, haemolysing 50% of the human erythrocytes (1% suspension in phosphate buffer saline) at a concentration of 1.6 µg/ml. Apers et al. (2001) also tested 10 novel saponins isolated from *Maesa lanceolata* for haemolytic activity. Some of the saponins showed no activity while others possessed very strong haemolytic activity. A number of structure–activity relationships were established and it was concluded that in the case of maesasaponins, substitution at position C-22 appears to be an essential structural feature for high haemolytic activity.

An oleanolic saponin mixture showed higher haemolytic activity than a dialysed reference saponin mixture from Merck® (HI 30 000) (Voutquenne et al., 2003). The saponins were isolated from the stem bark of *Pometia ridleyi* King emend. Radlk. (Sapindaceae). However, the quantities of pure saponins were insufficient to test individual haemolytic activities of each compound. Instead a saponin mixture was tested on sheep erythrocytes (10% suspension in phosphate buffer saline). A 70% haemolysis was obtained at 25 µg/ml. The HD₁₀₀ was obtained at 50 µg/ml and HD₅₀ was estimated at 23 µg/ml.

Ahn et al. (1998) investigated the inhibitory effect of *Bupleurum falcatum* L. (Apiaceae) saponins on anti-cell adhesive activity and its relation to haemolytic action. Saikosaponins-A, -D and -E were isolated and exhibited potent anti-cell adhesive activity and a strong haemolytic action. From the results, it was suggested that the mechanism

for anti-cell adhesive activity may resemble that for the haemolytic action.

2.2. Molluscicidal activity

Although toxic to cold-blooded species, if taken orally by warm-blooded species, saponins have only a weak toxicity (Bruneton, 1995), which is probably attributed to low absorption rates. The toxicity towards cold-blooded species has led to the use of saponin containing drugs to catch fish.

Saponins are also highly toxic to molluscs and have been investigated as molluscicides in the control of schistosomiasis (Sindambiwe et al., 1998; Abdel-Gawad et al., 1999). *Bulinus* and *Biomphalaria* species in particular, act as intermediate hosts in the life cycle of schistosomes, which cause urinary bilharzia. Many trials have been run in African countries where schistosomiasis has a high prevalence. In a study by Sindambiwe et al. (1998) a six-oleanane-type triterpenoid saponin mixture (maesasaponin mixture, isolated from *Maesa lanceolata*) was tested for molluscicidal activity against *Biomphalaria glabrata*. The saponin mixture showed high toxicity, with LD₉₅ and LD₅₀ values of 4.1 and 2.3 µg/ml, respectively.

Phytolacca dodecandra L'Hér. (Phytolaccaceae) and *Phytolacca icosandra* L. berries contain saponins with highly potent molluscicidal activity (Treyvaud et al., 2000). Aqueous extracts (25 µg/ml) of *Phytolacca icosandra* had a very high molluscicidal activity against *Biomphalaria glabrata* snails. According to Treyvaud et al. (2000), the activity can be attributed to the presence of monodesmosidic saponins of serjanic and spergulagenic acids. Mølgaard et al. (2000) investigated the biodegradability of molluscicidal water-extracted saponins from the berries of *Phytolacca dodecandra*. Results showed that the saponins in an aqueous extract of *Phytolacca dodecandra* readily biodegraded ($t_{1/2}$ = 15.8 h). The saponins were completely consumed within 10 days which indicates their abilities to degrade in aquatic environments under aerobic conditions. As a result, the use of *Phytolacca dodecandra* berries for snail control in schistosomiasis-infested water bodies is environmentally acceptable.

Apers et al. (2001) tested 10 saponins isolated from the leaves of *Maesa lanceolata* for molluscicidal activity against *Biomphalaria glabrata* snails. The LC₅₀ value of the saponin mixture was 1.25 mg/ml. However, it was concluded that one of the saponins, maesasaponin VI₂ is responsible for a large part of the activity of the mixture. This saponin had a LC₅₀ value of 0.5 mg/ml in its isolated form.

Triterpenoid hederagenin saponins isolated from *Sapindus mukorossi* Gaertn. (Sapindaceae) had molluscicidal effects against the golden apple snail, *Pomacea canaliculata*, which have become major pests of rice and other aquatic crops throughout Taiwan and other parts of Asia (Huang et al., 2003). Seven isolated hederagenin saponins, including one new hederagenin saponin, hederagenin 3-*O*-(2,4-*O*-di-acetyl- α -L-arabinopyranoside)-(1 \rightarrow 3)- α -L-rhamnopyranosyl-(1

\rightarrow 2)- α -L-arabinopyranoside, resulted in 70–100% mortality at 10 ppm against the golden apple snails. Hederagenin saponins with three sugar moieties had higher molluscicidal activity than triterpene saponins with one sugar moiety.

2.3. Anti-inflammatory activity

There are a number of reports of saponins with anti-inflammatory properties. Many saponins isolated from plant sources produce an inhibition of inflammation in the mouse carrageenan-induced oedema assay. In a study by Just et al. (1998), Fruticesaponin B, a bidesmosidic saponin with an unbranched saccharide moiety isolated from *Bupleurum fruticosum* L. (Apiaceae), was shown to have the highest anti-inflammatory activity of the all the saponins tested in the mouse oedema assays. Just et al. (1998) suggested that the anti-inflammatory activity of saponins isolated from *Bupleurum fruticosum* is related to the chemical structure of the saponins. In vivo studies on saponins isolated from *Bupleurum rotundifolium* L. (Apiaceae) were reported to have anti-inflammatory activity against both 12-*O*-tetradecanoylphorbol-13-acetate (TPA) induced ear oedema and chronic skin inflammation (Navarro et al., 2001). Of the seven saponins tested, five were fairly active in reducing the TPA-induced ear oedema. The saponins produced a dose-dependent oedema reduction. Only two saponins were active in reducing the chronic skin inflammation, and also caused a parallel decrease in neutrophil infiltration.

Aescin, a mixture of triterpenoid saponins that forms the major active principle of *Aesculus hippocastanum* L. (Hippocastanaceae), has been shown to have anti-inflammatory, anti-oedematous and venotonic properties (Sirtori, 2001).

Li et al. (2002) isolated two triterpenoid saponins from the stem bark of *Kalopanax pictum* Nakai (Araliaceae). Both kalopanaxsaponin A and pictoside A were isolated and showed significant anti-inflammatory activity at the oral dose of 50 mg/ml.

A novel steroidal saponin isolated from the leaves of *Agave attenuata* Salm-Dyck (Agavaceae) was evaluated for anti-inflammatory activity using the capillary permeability assay (da Silva et al., 2002). The steroidal saponin inhibited the increase in vascular permeability caused by acetic acid which is a typical model for the first stage inflammatory reaction. However, the activity was not accompanied by an undesirable haemolytic effect and warrants further investigation as an anti-inflammatory drug.

The triterpenoid saponin loniceroside C isolated from the aerial parts of *Lonicera japonica* Thunb. (Caprifoliaceae), a medicinal plant known as an anti-inflammatory agent for centuries, showed anti-inflammatory activity when tested in vivo in the mouse ear oedema provoked by croton oil (Kwak et al., 2003). Loniceroside C inhibited the ear oedema (15–31%) at concentrations ranging from 50–200 mg/kg.

Kim et al. (1998a) investigated the anticomplementary activity of ginseng (*Panax ginseng* C.A. Mey., Araliaceae)

saponins. Ginsenoside Ro and oleanolic acid showed the highest anticomplementary activity of the tested saponins. Kim et al. (1998a) suggested that the anti-inflammatory activity of these saponins is related to anticomplementary action through the classical inflammation pathway.

2.4. Antifungal/antiyeast activity

Sindambiwe et al. (1998) tested a maesasaponin mixture isolated from *Maesa lanceolata* for its fungistatic activity. The mixture inhibited the growth of *Epidermophyton floccosum*, *Microides interdigitalis* and *Trichophyton rubrum* at a concentration of 50 µg/ml. *Candida albicans* and *Microsporum canis* growth was inhibited at 100 µg/ml. The development of *Microsporum langeroni* was inhibited at 250 µg/ml. No fungicidal activity was shown at lower concentrations up to 1 µg/ml.

Saponins isolated from *Panax notoginseng* (Burk.) F.H.Chen (Araliaceae) were reported to exhibit an inhibitory effect on *Aphanomyces cochlioides* zoospore motility (Ma et al., 1999). Seven of the 14 saponins tested had an inhibitory effect on zoospore motility.

Li et al. (1999b) tested three jujubogenin saponins isolated from *Colubrina retusa* L. (Rhamnaceae) for antifungal activity against *Candida albicans*, *Cryptococcus neoformans* and *Aspergillus fumigatus*. The known saponin, jujubogenin [3-*O*- α -L-arabinofuranosyl-(1 \rightarrow 2)- β -D-glucopyranosyl-(1 \rightarrow 3)]- α -L-arabinopyranoside, showed modest growth-inhibitory effects with a MIC of 50 µg/ml against all three test cultures. Of the two new minor jujubogenin saponins isolated only one was marginally active with growth-inhibitory effects only against *Cryptococcus neoformans* (MIC = 50 µg/ml).

In a study by Bader et al. (2000) it was shown that antifungal activity of saponins against different *Candida albicans* strains can be influenced by the variation of the etherglycosidically bonded carbohydrate units and the acylglycosidically bonded oligosaccharide at C-28 of the aglycone.

Steroidal saponins from *Yucca schidigera* Roez. ex Ortgies (Agavaceae) (Mohave yucca) were shown to exhibit effective growth-inhibitory activities against food-deteriorating yeasts, film-forming yeasts, and dermatophytic yeasts and fungi (Miyakoshi et al., 2000). A saponin fraction, containing mainly monodesmosidic saponins, was tested for both antiyeast and antifungal activity. The saponin fraction showed growth-inhibitory activity against many of the yeasts, as well as some dermatophytic fungi (MIC values ranged between 31.3 and 125 µg/ml).

Eight previously characterized monodesmosidic saponins isolated from *Hedera colchica* K.Koch (Araliaceae) were tested for antifungal and antiprotozoal activity (Mshvildadze et al., 2000). Although the compounds exhibited antifungal activity, the activity was lower than those of the reference antifungal agents. However, even though the activity was low, there was a clear indication that the antifungal activity was structure related. Saponins with hederagenin as their

aglycone were more active than those without. The number, kind and sequence of the sugar residues also had a significant effect on the antifungal activity observed.

Triterpenoid saponins from the seeds of *Chenopodium quinoa* Willd. (Chenopodiaceae) have been reported to have antifungal activity (Woldemichael and Wink, 2001). Only the crude saponin mixture inhibited the growth of *Candida albicans* at 50 µg/ml. The pure compounds showed little or no activity, which suggests a possible synergistic effect between these saponins.

Furostanol saponins isolated from the seeds of *Capsicum annum* L. var. *acuminatum* Fingerh. (Solanaceae) showed stronger antiyeast activity than antifungal activity (Iorizzi et al., 2002). Three new furostanol saponins, capsicosides E, F and G, and seven oligoglycosides were isolated and tested for both antifungal and antiyeast activity. Antifungal MIC values ranged from 125 µg/ml to >1000 µg/ml and antiyeast MIC values from 12.5 to 10 µg/ml. However, when testing for novel pharmacological compounds, MIC values of >1000 µg/ml are generally too weak to be considered active and should rather be reported as “not active”.

Many different species of the genus *Phytolacca* (Phytolaccaceae) also contain saponins that show antifungal activity (Quiroga et al., 2001; Escalante et al., 2002). Three olean-type triterpenoid saponins isolated from the berries of *Phytolacca tetramera* Hauman (Phytolaccaceae) were tested for antifungal activity (Escalante et al., 2002). Two of the saponins, phytolaccosides B and E showed antifungal activity against the human pathogenic opportunistic fungi. Phytolaccoside B had the broadest spectrum of activity against the fungi tested.

CAY-1, a steroidal saponin isolated from the fruits of *Capsicum frutescens* L. (Solanaceae) was shown to be a potent fungicide and antiyeast properties (de Lucca et al., 2002). The saponins had LD₅₀ values between 3 and 20 µM against various *Aspergillus* species and IC₅₀ values of 9.5 µM and 6.2 µM against *Pneumocystis carinii* and *Candida albicans*, respectively. The results indicated that CAY-1 could prove to be an effective fungicide, at concentration levels that had no cytotoxic activity on A 549 lung carcinoma and HeLa cell lines.

Five new spirostanol saponins and two sterol glycosides isolated from *Solanum chrysotrichum* Schldh. (Solanaceae) leaves were tested for their antifungal activities (Zamilpa et al., 2002). One of the new spirostan saponins, 6 α -*O*- β -D-xylopyranosyl-(1 \rightarrow 3)- β -D-quinovopyranosyl-(25*R*)-5 α -spirostan-3 β ,23 α -ol, was the most active substance with MIC values of 100 and 200 µg/ml against *Aspergillus niger* and *Candida albicans*, respectively, and 12.5 µg/ml for both *Trichophyton mentagrophytes* and *Trichophyton rubrum*.

2.5. Antibacterial/antimicrobial activity

Saponins have also been reported to have antimicrobial activity (Killeen et al., 1998). Three butanol-extractable

5 β -spirostan-3 β -ol saponins were shown to have antimicrobial activity on both prokaryotic and eukaryotic organisms, but only at low cell densities. The saponins did not inhibit microbial growth of dense populations.

Three new triterpenoid saponins, Nudicaucins A, B, and C and a known saponin guaiacin D were isolated from *Hedyotis nudicaulis* Wight & Arn. (Rubiaceae) were tested against *Bacillus subtilis* (Konishi et al., 1998). All four of the isolated saponins showed weak antibacterial activity. Results indicated that the tetraglycoside saponins have stronger activity than the triglycoside saponins.

A new jujubogenin saponin isolated from *Colubrina retusa* L. (Rhamnaceae), jujubogenin 3-*O*- α -L-arabinofuranosyl-(1 \rightarrow 2)-[3-*O*-(*trans*)-*p*-coumaroyl- β -D-glucopyranosyl-(1 \rightarrow 3)]- α -L-arabinopyranoside, had antimycobacterial activity when tested against *Mycobacterium intracellulare* (ElSohly et al., 1999). The jujubogenin saponin had antimycobacterial activity at a MIC of 10 μ g/ml.

Iorizzi et al. (2002) isolated three new furostanol saponins along with seven known saponins from the seeds of *Cap-sicum annuum* L. var. *acuminatum* Fingerh. (Solanaceae). The saponins showed weak or no growth inhibition against both Gram-positive and Gram-negative bacteria (MIC >1000 μ g/ml).

2.6. Antiparasitic activity

Two new triterpenoid saponins, glinoside A and B, isolated from the aerial parts of *Glinus oppositifolius* L. (Molluginaceae) were shown to have antiprotozoal activity against *Plasmodium falciparum* (Traore et al., 2000). Results showed that the saponin fractions had slightly better antiplasmodial activity (IC₅₀ of 31.8 μ g/ml) than pure glinoside A (IC₅₀ of 42.3 μ g/ml).

Three saponins isolated from *Hedera helix* L. (Araliaceae), α - and β -hederin and hederacolchiside A₁, were shown to have antileishmanial activity (Delmas et al., 2000). The results showed that these saponins exhibited a strong antiproliferative action on all the stages of development of the parasite *Leishmania infantum*. The action of the saponins was due to changes in membrane integrity and potential. Hederacolchiside A₁ had the strongest activity against both promastigote (IC₅₀ of 1.2 \pm 0.1 μ M) and amastigote (IC₅₀ of 0.053 \pm 0.002 μ M) form of the parasite. The same saponins also exhibited potent antiproliferative activity against human monocytes as a result of significant DNA synthesis inhibition. The findings suggest that these saponins could be considered as possible future antileishmanial drugs.

2.7. Cytotoxicity and antitumor activity

Numerous reports highlight the highly cytotoxic properties of many saponins. However, saponins with high cytotoxicity do not always have antitumor properties as cytotoxic compounds can potentially be used as antitumor agents.

A novel steroidal saponin, furcreastatin, isolated from an ethanolic extract of the leaves of *Furcraea foetida* (L.) Haw. (Agavaceae) was screened for its selective cytotoxicity towards mutant p53-expressing mouse fibroblasts (Itabashi et al., 1999). Furcreastatin consists of a hecogenin aglycone with a hexasaccharide containing D-galactose, L-rhamnose and four D-glucose residues. The compound decreased the viability of mutant p53-overexpressing cells with an ED₅₀ of 4 μ g/ml. Furcreastatin was also reported to be cytotoxic against parental cell-lines (ED₅₀ of 9.6 μ g/ml).

Many isolated steroidal saponins have been shown to be either cytostatic or cytotoxic to HL-60 human leukemia cell lines (Mimaki et al., 1998b, 1998c, 1999a, 1999c, 2001b; Yokosuka et al., 2002b). Mimaki et al. (1998b) tested 11 new saponins isolated from *Ruscus aculeatus* L. (Liliaceae). Only two of these saponins, ruscogenin diglycoside (spirostanol saponin) and its corresponding 26-glycosyloxyfurostanol saponin showed cytostatic activity at 10 μ g/ml (IC₅₀ values 3.1 and 3.7 μ g/ml, respectively).

Mimaki et al. (1999c) also tested nine steroidal saponins, including five new saponins, isolated from the aerial parts of *Dracaena draco* L. (Dracaenaceae) for their cytostatic activities. Only two of the tested saponins showed relatively potent cytostatic activity against the human promyelocytic leukemia HL-60 cells. Only one of the new saponins, (23*S*,24*S*)-spirosta-5,25(27)-diene-1 β ,3 β ,23,24-tetrol-1-*O*-[*O*-(2,3,4-tri-*O*-acetyl- α -L-rhamnopyranosyl)-(1 \rightarrow 2)- α -L-arabinopyranosyl]24-*O*- β -D-fucopyranoside, and the known compound, (25*R*)-spirost-5-en-3 β -ol-3-*O*-[*O*- α -L-rhamnopyranosyl-(1 \rightarrow 2)- β -D-glucopyranoside], had cytostatic activities with IC₅₀ values of 2.6 μ g/ml and 1.3 μ g/ml, respectively. Tran et al. (2001b) tested spirostanol and furostanol type saponins from the roots and rhizomes of *Dracaena angustifolia* Roxb. (Dracaenaceae) for antiproliferative activity against murine colon 26-L5 carcinoma, human HT-1080 fibrosarcoma, and B-16 BL6 melanoma cells. Three of the tested compounds showed potent antiproliferative activity against HT-1080 fibrosarcoma cells (IC₅₀ values from 0.2 to 0.6 μ M). Draconins A, B and C, three new steroidal saponins, were isolated from the stem bark of *Dracaena draco* along with 17 known compounds (González et al., 2003). Several of the isolated compounds showed potent cytotoxic activity against the human leukemia cell line HL-60 (IC₅₀ values from 2.0 to 9.7 μ M at 72 h).

Triterpenoid saponins have also shown cytotoxicity against human cell lines. A novel triterpene saponin, isolated from the root bark of *Aralia dasyphylla* Miq. (Araliaceae) showed significant cytotoxic activity against KB and HeLa-S₃ cells (Xiao et al., 1999). The IC₅₀ values were 1.2 μ g/ml for KB cells and 0.02 μ g/ml for HeLa-S₃ cells.

Lee et al. (1999) isolated a novel saponin metabolite (IH-901) from *Panax ginseng* C.A.Meyer (Araliaceae), which showed in vitro antitumor activity. This compound was tested against four human cancer cell lines and one subline resistant to cisplatin (CDDP). From the results it was suggested that this saponin was not cross-resistant to

be administered safely as anticancer agents due to their non-toxic and non-haemolytic properties. Yun (2003) also investigated the anticancer properties of *Panax ginseng* C.A.Meyer (Araliaceae). From the study it was concluded that the activity of ginseng saponins are non-organ specific and that the anticarcinogenicity or human cancer preventative effect of *Panax ginseng* is due to the ginsenoside saponins Rg₃, Rg₅ and Rh₂.

Mimaki et al. (1999a) tested nine triterpene saponins isolated from the roots of *Pulsatilla chinensis* (Bunge) Regel (Ranunculaceae) for their cytotoxic activity. All the saponins tested exhibited moderate cytotoxic activity with IC₅₀ values ranging from 2.3 to 7.8 µg/ml, with exception of one saponin which had no substituent at C-2 of the arabinosyl moiety attached to the aglycone. The results of the testing suggested that the glycoside moiety attached at the C-3 of the aglycone is essential for cytotoxic activity from the saponins evaluated.

Cytotoxic triterpenoid saponins were isolated from a methanol extract of the aerial parts of *Trevesia palmata* (Roxb. ex Lindl.) Vis. (Araliaceae) (De Tommasi et al., 2000). Six new bisdesmosidic saponins, along with two known triterpenoid saponins, were tested for their antiproliferative activities against three continuous culture cell lines (J774, HEK-293 and WEHI-164). Results of this investigation showed that the hydroxyl group at C-28 and the saccharide chain esterified at C-28 play an important role in mediating antiproliferative activity.

Two new triterpenoid saponins isolated from the roots of *Acanthophyllum squarrosum* Boiss. (Caryophyllaceae) were tested in vitro for lymphocyte antiproliferation (Gaidi et al., 2000b). The results revealed one of the saponins to have a moderate concentration-dependent cytotoxic effect on lymphocytes in culture. The same saponin was not cytotoxic to lymphocytes up to a concentration of 10 µg/ml, although higher concentrations showed strong cytotoxicity.

Ginseng (*Panax ginseng* C.A.Meyer, Araliaceae) saponins were shown to have antiproliferative effects on human prostate cancer cell lines (Liu et al., 2000). One of the tested ginsenosides, ginsenoside Rg₃, displayed growth inhibitory activity against human prostate carcinoma LNCaP cells. The ginsenoside Rg₃ activated the expression of cyclin-kinase inhibitors, p21 and p27, arrested LNCaP cells at the G1 phase, and subsequently inhibited tumor cell growth through a caspase-3-mediated apoptosis mechanism.

Qiu et al. (2000) isolated the saponin chloromaloside A from *Chlorophytum malayense* Ridl. (Liliaceae), which was found to be highly cytotoxic. In vitro studies showed this steroidal saponin to have cytotoxicity against human cancer cell lines.

of *Albizia subdimidiata* (Splitg.) Barneby & J.W. Grimes (Leguminosae) for their cytotoxic activity. Both saponins showed significant cytotoxicity against A2780 cells. One of the compounds, albiziatrioside A, is a new triterpenoid saponin and had an IC₅₀ value of 0.9 µg/ml.

In a study by Yokosuka et al. (2000a) nine isolated steroidal saponins, including three new bisdesmosidic spirostanol saponins, surculosides A, B and C and one bisdesmosidic furostanol saponin, were tested for cytotoxic activity against HL-60 human promyelocytic leukemia cells. Only the three known saponins of the nine tested, showed weak cytotoxic activity with their IC₅₀ values ranging from 4.2 to 8.7 µg/ml.

Eight steroidal saponins isolated from *Allium porrum* L. (Alliaceae) were found to be cytotoxic to WEHI 164 cells (IC₅₀ values from 1.9 to 21.1 µg/ml) and J774 cells (IC₅₀ values from 2.1 to 27.9 µg/ml) (Fattorusso et al., 2000). Three of the tested saponins had IC₅₀ values below 6 µg/ml against both cell lines. Baba et al. (2000) showed saponins isolated from another *Allium* species, *Allium chinense* G.Don (Alliaceae), to have antitumor-promoting activity in a two-stage lung carcinogenesis experiment.

Two triterpene saponins, securioside A and securioside B; were isolated from a saponin fraction of an aqueous extract of *Securidaca inappendiculata* Hassk. (Polygalaceae) roots (Yui et al., 2001). The saponin fraction inhibited macrophage growth as a result of a cytotoxic effect. It was suggested that these two saponins are essential for the cell death-inducing activity of the aqueous extract.

Dong et al. (2001a, 2001b) showed steroidal saponins isolated from *Dioscorea panthaica* Prain & Burkill (Dioscoreaceae) to be cytotoxic to A375-S2, L929 and HeLa cell lines. All seven of the isolated saponins tested had cytotoxic activities against the three cell lines (Dong et al., 2001a). The IC₅₀ values ranged from 8.4 to 2.2 µg/ml against A375-S2 cells, 8.6 to 1.8 µg/ml against L929 cells and 7.9 to 2.1 µg/ml against HeLa cell line. Dioscin, a known saponin had the most potent cytotoxic activity against all the cell lines (Dong et al., 2001a).

Saponins isolated from *Camassia leichtlinii* (Bak.) S. Wats. (Liliaceae) have been shown to have cytotoxic activity against human oral squamous cell carcinoma (HSC-2) cells and normal human gingival fibroblasts (Kuroda et al., 2001).

Hederagenin, α -hederin, kalopanaxsaponin A (commonly known as α -hederin), kalopanaxsaponin I, and sapindoside C were isolated from the stem bark of *Kalopanax pictus* Nakai (Araliaceae) (Park et al., 2001). These saponins were tested for their cytotoxicity against different types of tumor cells. The results indicated that kalopanaxsaponin A has potential antitumor applications. In vivo studies on antitumor activity

CDDP in the tested cell line and could be a candidate for the treatment of CDDP resistant pulmonary cancer. Ginseng saponins isolated from *Panax ginseng* C.A.Meyer (Araliaceae) and their cancer preventing activities were reviewed by Shibata (2001). It was concluded that ginsenoside tetraolide desacetyone and ginsenoside Rg3 were

Julibroside J₁ and Julibroside J₉, two diastereomeric saponins isolated from the stem bark of *Albizia julibrissin* Durazz. (Leguminosae), showed cytotoxic activity (Zou et al., 2000). Both saponins showed good inhibitory action against the KB cancer cell lines in vitro. Abdel-Kader et al. (2003) isolated and isolated saponins from a methanol extract

by ethanol extracts of *Nigella sativa* L. (Ranunculaceae) seeds have shown the principle bioactive compound to be α -hederin, a monodesmosidic triterpene saponin (Kumara and Huat, 2001).

Mimaki et al. (2001a) tested steroidal saponins isolated from the leaves of *Cestrum nocturnum* L. (Solanaceae) for their cytotoxic activities against human oral squamous cell carcinoma (HSC-2) cells and normal human gingival fibroblasts (HGF). The steroidal saponins exhibited considerable cytotoxicity against HSC-2 cells, with LD₅₀ values ranging from 2.0 to 13 μ g/ml. Three of the saponins showed 5–10-fold higher cytotoxic activities against HSC-2 cells than against HGF. However, two compounds were cytotoxic against both HSC-2 cells and HGF. Mimaki et al. (2001a) concluded that the structure of the sugar portion of these steroidal saponins appears to play an important role in tumor-specific cytotoxicity.

Mimaki et al. (2001b) systematically examined the cytotoxic activities of a number of steroidal saponins isolated from plants of the Liliaceae family. Some of the saponins showed potent cytotoxic activity against HL-60 human promyelocytic leukemia cells. The cytotoxic activity was found to be linked to the monosaccharides constituting the sugar moieties and their sequences, as well as to the structure of the aglycones.

Hederacolchiside A₁, a new oleanolic acid monodesmoside isolated from *Hedera colchica* K.Koch (Araliaceae) demonstrated strong cytotoxicity activities on a number of cancer cells (IC₅₀ from 4.5 to 12 μ M) (Barthomeuf et al., 2002). The antiproliferative effects on the different cancer lines suggests that despite the lack of specificity for cancer cells, hederacolchiside A₁ has potential antitumor applications.

Triterpene saponins isolated from *Silene fortunei* Vis. (Caryophyllaceae) were shown to increase the accumulation and cytotoxic activity of the anticancer agent cisplatin on human colon tumor cells (Gaidi et al., 2002). On their own, the saponins did not have significant cytotoxic activities.

Four new steroidal saponins were isolated from rhizomes of *Tacca chantrieri* André (Taccaceae) (Yokosuka et al., 2002b). The isolated compounds were evaluated for their cytotoxic activity against HL-60 human promyelocytic leukemia cells. One of these compounds showed considerable cytotoxicity (IC₅₀ of 1.8 μ M). Two other saponins, which were structurally related to the active saponin, did not show cell growth inhibitory activity when tested at 10 μ g/ml. These findings suggest that both the aglycone structure and the sugar moieties contribute to the cytotoxicity activity of the saponins. Even slight structural differences can affect the activity.

Seo et al. (2002b) isolated three new saponins and three known saponins from *Acacia tenuifolia* (L.) Willd. (Leguminosae) using bioassay-guided fractionation. The saponins showed weak activity against the genetically engineered *Saccharomyces cerevisiae* mutant (1138, 1140, 1353 and Sc-7) yeast strains tested. Two of the known saponins, which were

previously isolated by Abdel-Kader et al. (2001), showed significant cytotoxic activity against M 109 lung cancer cell lines, with IC₅₀ values of 1 μ M. The new saponins had weak activity against the A 2780 ovarian cancer cell lines. Another *Acacia* species, *Acacia victoriae* Benth. (Leguminosae), contains saponins with tumor-inhibitory activity (Jayatilake et al., 2003). Two new saponins, Avicins D and G, were isolated from the seedpods of *Acacia victoriae*. Both compounds showed potent cytotoxic activity against human T-cell leukemia (Jurkat cells) in vitro. Avicin D and Avicin G had IC₅₀ values of 0.58 μ g/ml and 0.22 μ g/ml, respectively. Mujoo et al. (2001) investigated the antiproliferation effect of triterpenoid saponins isolated from *Acacia victoriae*. The saponins and avicins markedly inhibited the growth of several tumor cell lines with low growth inhibition in human foreskin fibroblasts, mouse fibroblasts and immortalized breast epithelial cells at similar concentrations. Hanausek et al. (2001) tested the ability of avicin saponins from *Acacia victoriae* to inhibit chemically induced mouse skin carcinogenesis. The results suggest that these compounds could be potential suppressors of the development of human skin cancer and other epithelial malignancies. Three new saponins, isolated from the fruits of *Acacia concinna* Wall. (Leguminosae), were tested for cytotoxic activity against human HT-1080 fibrosarcoma cells (Tezuka et al., 2000). All three saponins, kinmoonosides A, B and C exhibited significant cytotoxicity with ED₅₀ values of 0.7, 0.91 and 2.83 μ M, respectively. It is thought that the ester moiety found at C-21 of the aglycone is not crucial for the cytotoxicity but may rather intensify the activity.

Another novel triterpenoid saponin, pittoviridoside, was isolated from *Pittosporum viridiflorum* Sims (Pittosporaceae) using bioassay-guided fractionation with genetically engineered *Saccharomyces cerevisiae* mutant yeast strains (1138, 1140, 1353 and Sc-7) (Seo et al., 2002a). The compound was shown to have both weak cytotoxicity activity against A 2780 human ovarian cancer cell lines (IC₅₀ 10.1 μ g/ml) and weak activity against yeast strains.

Mixtures of saponins have also been shown to have cytotoxic activities. Marquina et al. (2001) reported on a mixture of monodesmoside saponins, which were not active as pure compounds, to be highly cytotoxic against P388 and colon cell lines (ED₅₀ values of 2.3 and 3.6 μ g/ml, respectively).

2.8. Antiviral activity

Saponins have also been reported to have antiviral activities. Simões et al. (1999) tested two triterpenoid saponins isolated from Brazilian and Chinese plants for their antiviral activity. Both triterpenoid saponins exhibited antiviral activity. The oleanane-type inhibited herpes simplex virus type 1 DNA synthesis, while the ursane-type saponin inhibited viral capsid protein synthesis of herpes simplex virus type 1.

Triterpenoid saponins from the Fabaceae family have been reported to have anti-herpes virus activity (Kinjo et al., 2000). Anti-herpes simplex virus activity was found to be

structure related. Saponins having a glucosyl unit in the central sugar moiety seemed to show greater activity.

Triterpenoid saponins isolated from the leaves of *Maesa lanceolata* Forssk. (Myrsinaceae) were tested for structure–activity relationships against HSV-1 (for extracellular virucidal activity) and HIV viruses (Apers et al., 2001). It was concluded that a free 16-OH and acylation of the 22-OH appears to be essential for antiviral activity. These saponins, however, showed no anti-HIV activity and it was concluded that the cytotoxicity of the compounds were more pronounced than a potential antiviral effect.

Arganine C, a saponin isolated from the fruits of *Tieghemella heckelii* Pierre ex A.Chev. (Sapotaceae) was reported to have antiviral activity (Gosse et al., 2002). The saponin, strongly inhibited the entry of HIV into cells in a cell fusion assay, and showed no significant cytotoxicity towards HeLa-CD4⁺ cells.

A mixture of tea-seed saponins from *Camellia sinensis* L. var *sinensis* (Ternstroemiaceae), were reported to inactivate human type A and B influenza viruses. However, these saponins were also toxic to the host cells and further studies need to be conducted (Hayashi et al., 1999).

The maesasaponin mixture isolated from *Maesa lanceolata* Forssk. (Myrsinaceae) was reported to have both anti-herpes simplex virus type 1 (HSV-1) and poliovirus type 1 activity (Sindambiwe et al., 1998). The saponin mixture reduced the HSV-1 infectivity at a concentration of 100 µg/ml and inactivated the Herpes simplex virus at 250 µg/ml.

Escin saponins isolated from the seeds of *Aesculus chinensis* Bunge (Hippocastanaceae) were tested for HIV-1 protease inhibition (Yang et al., 1999). Eight saponins were tested, four of which were novel compounds. The escin saponins inhibited $86.1 \pm 0.2\%$ of the HIV-1 protease activity at a concentration of 100 µM. A mixture of the saponin escin Ia and escin Ib showed $89.9 \pm 1.1\%$ inhibitory activity against HIV-1 protease at 100 µM. Escin Ia and escin Ib showed inhibitory activity against HIV-1 protease with IC₅₀ values of 35 µM and 50 µM, respectively.

2.9. Other biological activities

The roots of *Panax* species (ginseng) have been found to contain a series of tetracyclic triterpenoid saponins which make up the active ingredients. The saponin content is said to vary between different *Panax* species (Nocerino et al., 2000). Ginseng saponins have been shown to have a wide variety of biological properties. The aphrodisiac and adaptogenic properties of *Panax quinquefolium* L. (Araliaceae) and *Panax ginseng* C.A.Meyer were reviewed by Nocerino et al. (2000). It was concluded that when used appropriately, ginseng appears to be safe, but side effects are documented. Attele et al. (1999) reviewed selected effects of *Panax* species and their major active steroidal saponin components. The structure–function relationship and potential targets of action were discussed. The ability of ginsenosides to independently target multireceptor systems at the

plasma membrane and activate intracellular steroid receptors is thought to explain their pharmacological effects.

Saponins from Ginseng Radix rubra (*Panax ginseng* C.A.Meyer, Araliaceae) were shown to have an effect on wound healing (Kanzaki et al., 1998). The study involved examining the effects of saponin on the extracellular matrix metabolism, the activation and synthesis of TGF-β1, and the modification of TGF-β receptor expressions in fibroblasts in order to clarify the contribution of the TGF-β pathway to the mechanism of wound healing. It was concluded that saponin stimulates the wound healing process through changes of the extracellular matrix metabolism and is accompanied by modification of TGF-β receptor expressions in fibroblasts.

Huong et al. (1998a) investigated the antioxidant activity of Vietnamese ginseng (*Panax vietnamensis* Ha & Grushv., Araliaceae) saponins. The results of the study showed that Vietnamese ginseng saponins exert protective action against free radical-induced tissue injury. However, the activity is attributed to the minor saponin components rather than the major saponin components.

Korean red ginseng (*Panax ginseng* C.A.Meyer, Araliaceae) saponins were also found to have an effect on ethanol-induced amnesia (Lee et al., 2000). Jin et al. (1999) also worked on two Korean red ginseng saponins, protopanaxadiol and protopanaxatriol, and their effect in different ratios on scopolamine-induced learning ability and spatial working memory in mice. The two saponins improved the scopolamine-induced learning impairment at different dosages in the mice. However, neither of the saponins showed a favorable effect on learning and memory in normal mice. Different ratios of the two saponins were shown to have different effects. A low protopanaxadiol/protopanaxatriol ratio improved the spatial working memory of the mice. The reverse showed no improvement suggesting that the protopanaxadiol/protopanaxatriol ratio of ginseng saponins may play an important role in the pharmacological effect of red ginseng. Une et al. (2001) investigated the effect of saponins on cognitive behaviour and anxiety in albino mice. The saponin mixture isolated from *Albizia lebbek* Willd. (Leguminosae) significantly improved the retention ability of the normal and amnesic mice as compared to the respective controls.

Kim et al. (1998b) showed the effect of ginseng total saponin from the root of *Panax ginseng* C.A.Meyer (Araliaceae) on morphine-induced hyperactivity and conditioned place preference in mice. An intraperitoneal injection of ginseng total saponin prior to, and during the morphine treatment in mice inhibited morphine-induced hyperactivity and conditioned place preference. A single dose of ginseng total saponin also inhibited apomorphine-induced climbing behaviour which shows the antidopaminergic action of the saponins at the postsynaptic dopamine receptor.

In another study by Kim et al. (1999) the administration of ginseng total saponin prior to and during the nicotine treatment in mice inhibited, not only nicotine-induced hyperac-

tivity and conditioned place preference, but also postsynaptic dopamine receptor supersensitivity in nicotine-induced conditioned place preference mice. The results suggest that ginseng total saponin may be useful for the prevention and therapy of some of the adverse effects of nicotine.

A new oleanene-type saponin isolated from the flowers of *Spartium junceum* L. (Leguminosae) showed potent anti-ulcerogenic activity (Yeşilada and Takaishi, 1999). The saponin named spartitrioside exerted a potent effect against ethanol-induced gastric lesions in rats. The activity was more effective than the reference compound, famotidine.

Saponins isolated from *Polygala senega* L. (Polygalaceae) had potential vaccine adjuvant activity, increasing specific immune responses in mice immunized with ovalbumin and hens immunized with rotavirus (Estrada et al., 2000). The saponins increased specific antibody levels to the antigens in both the mice and hens. Saponins as potential adjuvants for orally-administered vaccines were reviewed by Sjölander and Cox (1998). Special reference was made to the induction of local and systemic immune responses and interactions with the internal epithelium. Barr et al. (1998) also reviewed the adjuvant activity of saponins. Saponins from *Quillaja saponaria* Molina (Rosaceae) and the relationships between adjuvant activity, toxicity and saponin structure were reviewed. Oda et al. (2003) also examined the relationship between adjuvant activity and saponin structure. The correlation between adjuvant activity and the amphipathic structure of soyasaponins was investigated. It is thought that the amphipathic structure may indeed define the fundamental adjuvanticity of saponins. In a brief overview by Kersten and Crommelin (2003) of iscoms which have built-in adjuvants in the form of *Quillaja* saponin, recent research on the use of better defined saponin adjuvants were discussed. According to Johansson and Lövgren-Bengtsson (1999) iscoms that are made up of different defined fractions of quillaja saponins, exhibit different immunomodulatory activities when tested for serum antibody responses.

Triterpenoid saponins from the roots and flower buds of *Panax notoginseng* (Burk.) F.H.Chen (Araliaceae) showed potent hepatoprotective effects on liver injury induced by D-galactosamine and lipopolysaccharide (Yoshikawa et al., 2003). The major saponins isolated from the buds, ginsenosides-Rb₃ and -Rc, showed stronger hepatoprotective activity than the major saponins isolated from the roots, ginsenoside-Rb₁ and -Rg₁. Sixteen triterpenoid saponins from *Panax vietnamensis* Ha & Grushv. (Araliaceae) were also found to possess hepatocytotoxic effects on D-galactosamine/tumor necrosis factor- α -induced cell death in primary cultured mouse hepatocytes (Tran et al., 2001a). From these results it was concluded that the hepatocytotoxic effect of Vietnamese ginseng is due to dammarane-type triterpene saponins that have an ocotillol-type side chain. Tran et al. (2002) investigated the hepatocytotoxic effect of majonoside R₂ the major saponin constituent from *Panax vietnamensis*. The saponin was tested in vivo on

D-galactosamine/lipopolysaccharide-induced hepatic apoptosis and subsequent liver failure in mice. Majonoside R₂ was found to protect primary cultured mouse hepatocytes from cell death by inhibiting the induced apoptosis. Majonoside-R₂, was also investigated for its effect on behavioural and pathophysiological changes caused by psychological stress (Huong et al., 1998b). Majonoside-R₂ attenuated communication box paradigm-induced psychological stress (CBP stress) and conditioned fear stress-induced antinociception, and had a protective effect against CBP stress-induced gastric lesions. The saponin also restored the hypnotic activity of pentobarbital to levels similar to the unstressed controls. Saponins from different *Panax* species have been reported to demonstrate a number of actions on the central nervous system. Results from studies done on saponins isolated from *Panax japonicus* C.A.Meyer (Araliaceae), indicate that these saponins may be useful in the treatment of neurodegenerative diseases (Zou et al., 2002a). Four new isolated yesaninoside saponins together with nine ginsenosides were tested. Ginsenosides Rb₁ and Rb₄ and notoginsenosides R₄ and Fa were shown to have significant neurite outgrowth activity in human neuroblastoma SK-N-SH cells. These saponins were also found to significantly increase the total length of the neurites and the number of varicosities per cell. Ginsenosides Rb₁ and Rb₄ increased the total length of neurites by more than three times the control. Liao et al. (2002) also investigated the effect of saponins (ginseng total saponin) on neurological disorders. The neuroprotective effects of ginseng total saponin and ginsenosides Rb₁ and Rg₁ on spinal cord neurons were investigated. In vitro studies revealed ginsenosides Rb₁ and Rg₁, isolated from the roots of *Panax ginseng* C.A.Meyer (Araliaceae), as efficient neuroprotective agents. The saponins protected the spinal neurons from excitotoxicity induced by glutamate and kainic acid, as well as oxidative stress induced by hydrogen peroxide. The effects were shown to be dose dependent, with the optimal dose of 20–40 μ M to be most effective.

In a study by Herlt et al. (2002), two major saponins, 3-O-[[β -D-galactopyranosyl-(1 \rightarrow 3)- β -D-glucopyranosyl(1 \rightarrow 2)]- β -D-glucuronopyranosyloxy}-22-O-(2-methylbutyryloxy)-15,16,28-trihydroxy-(3 β ,15 α ,16 α ,22 α)-olean-12-ene and 3-O-[[β -D-galactopyranosyl(1 \rightarrow 3)- β -D-glucopyranosyl(1 \rightarrow 2)]- β -D-glucuronopyranosyloxy}-22-O-(2(E)-methyl-2-butenyloxy)-15,16,28-trihydroxy-(3 β ,15 α ,16 α ,22 α)-olean-12-ene, were isolated from the seeds of *Barringtonia asiatica* Kurz (Lecythidaceae) and tested for antifeedant properties towards *Epilachna* larvae. The saponins were tested at concentrations of 1000, 500, 100 and 50 μ g/ml on *Solanum nigrum* leaves. The results showed the saponin containing tiglate to have considerably higher antifeedant activity than the saponin containing 2-methylbutyrate. At a concentration of 100 μ g/ml, the tiglate-containing saponin had 39% antifeedant activity and the 2-methylbutyrate-containing saponin had 0% activity.

Three novel ginseng saponin metabolites formed by intestinal bacteria were evaluated for their antigenotoxic properties (Lee et al., 1998). The compounds inhibited benzopyrene-induced mutagenicity in a dose-dependent manner. It was suggested that the results indicate that these ginseng saponin metabolites could have potential as chemopreventive agents. Scarpato et al. (1998) investigated the effects of isolated saponins from *Bupleurum fruticosum* L. (Apiaceae) on the clastogenicity and cytotoxicity of the anticancer drugs mitomycin C and bleomycin. One of the saponins showed a dose-dependent mitomycin C-induced mutagenesis inhibition and a co-genotoxic effect on bleomycin-treated cultures. Soybean (*Glycine max* Merrill., Leguminosae) extracts have been shown to repress induced genomic DNA damage, cell clastogenicity and point mutation in cultured mammalian cells. Berhow et al. (2000) showed that a mixture of soyasaponins repressed 2-acetoxyacetylaminofluorene (2AAAF)-induced DNA damage in Chinese hamster ovary cells. Soyasapogenol B aglycone showed significant antigenotoxic activity against 2AAAF. These results are the first to demonstrate the antimutagenic activity of soybean saponins in mammalian cells. Yoshiki et al. (1998) reviewed the relationship between the chemical structure and biological activities of triterpenoid saponins isolated from *Glycine max* Merrill. (Leguminosae).

Saponins isolated from the roots of *Zygophyllum gaetulum* Emb. & Maire (Zygophyllaceae) were tested for their effects on electrically-stimulated guinea-pig ileum (Aquino et al., 2001). The results showed that the saponin zygophylloside N significantly reduced the electrically-induced contractions. The antispasmodic activity shown by this saponin was dose-dependent.

In a study by Parab and Mengi (2002) saponins extracted from *Acorus calamus* L. (Araceae) were tested for hyperlipidemic activity. Treatments of hyperlipidemic rats with saponins (10 mg/kg) significantly decreased the serum cholesterol and triglyceride levels. However, neither of the lipoprotein levels were brought down to baseline values, but it was still concluded that the saponins contribute to the hypolipidemic activity of *A. calamus*. Saponin fractions from *Allium* species have been shown to decrease the plasma total cholesterol levels (Matsuura, 2001). The active fractions contained steroid saponins which are thought to be responsible for the cholesterol lowering effects of garlic. In a minireview of natural products and their biological activities, saponins were listed under compounds with hypocholesterolemic activity (Wang and Ng, 1999).

3. Distribution of saponins

Saponins are found in a wide variety of foods including asparagus, beans, blackberries, peas, potatoes, sugar beet and tea (Dini et al., 2001a). They occur in many different plant families, as evidenced by the isolation of saponins from phytochemical studies of many plant species over the years. Table 1 provides a list of species from which saponins have been isolated in the last 5 years (1998–2003). Although this list is not exhaustive, it does give a good indication of the plant species and families which have formed the focus of research in saponin chemistry in recent years. Many of these species have been chosen for phytochemical research based on ethnobotanical use. Of the roughly 200 species listed, 40% of the species were investigated based on their traditional usage. Two triterpenoid saponins, eliciting

Table 1

A list of plant species from which saponins have been isolated in recent years (1998–2003)

Family	Species	Saponin type	Reference
Agavaceae	<i>Agave americana</i> L.	Steroid	Yokosuka et al., 2000a
	<i>Agave attenuata</i> Salm-Dyck	Steroid	da Silva et al., 2002
	<i>Agave decipiens</i> Baker	Steroid	Abdel-Gawad et al., 1999
	<i>Cordyline stricta</i> (Sims) Endl.	Steroid	Mimaki et al., 1998d
	<i>Furcraea foetida</i> (L.) Haw.	Steroid	Itabashi et al., 1999
	<i>Yucca filamentosa</i> L.	Steroid	Plock et al., 2001
	<i>Yucca schidigera</i> Roezl. ex Ortgies	Steroid	Miyakoshi et al., 2000
			Oleszek et al., 2001
	<i>Allium chinense</i> G.Don	Steroid	Baba et al., 2000
	<i>Allium karataviense</i> Regel	Steroid	Mimaki et al., 1999b
Alliaceae	<i>Allium mutans</i> L.	Steroid	Akhov et al., 1999
	<i>Allium porrum</i> L.	Steroid	Carotenuto et al., 1999
			Fattorusso et al., 2000
	<i>Allium triquetrum</i> L.	Steroid	Corea et al., 2003
	<i>Allium tuberosum</i> Rottl. ex Spreng.	Steroid	Sang et al., 1999a, 1999b, 2001a, 2001b
			Zou et al., 2001

Table 1 (Continued)

Family	Species	Saponin type	Reference
Amaranthaceae	<i>Achyranthes aspera</i> L.	Triterpenoid	Kunert et al., 2000
	<i>Achyranthes bidentata</i> Blume	Triterpenoid	Michl et al., 2000
	<i>Alternanthera repens</i> (L.) Link	Triterpenoid	Mitaine-Offier et al., 2001a, 2001b
	<i>Amaranthus caudatus</i> L.	Triterpenoid	Sanoko et al., 1999
	<i>Amaranthus cruentus</i> L.	Triterpenoid	Rastrelli et al., 1998
Apiaceae (Umbelliferae)			Junkuszew et al., 1998
			Oleszek et al., 1999
	<i>Bupleurum falcatum</i> L.	Triterpenoid	Ahn et al., 1998
	<i>Bupleurum frutescens</i> L.	Triterpenoid	Just et al., 1998
	<i>Bupleurum rigidum</i> L.	Triterpenoid	Sánchez-Contreras et al., 1998, 2000
	<i>Bupleurum rotundifolium</i> L.	Triterpenoid	Navarro et al., 2001
	<i>Bupleurum scorzoniferifolium</i> Willd.	Triterpenoid	Fujioka et al., 2003
Aquifoliaceae	<i>Centella asiatica</i> (L.) Urb.	Triterpenoid	Li et al., 1999a
			Matsuda et al., 2001
	<i>Ilex amara</i> (Vell.) Loës.	Triterpenoid	de Andrade et al., 2002
	<i>Ilex kudincha</i> C.J.Tseng	Triterpenoid	Nishimura et al., 1999
Araliaceae	<i>Ilex latifolia</i> Thunb.	Triterpenoid	Huang et al., 2001a, 2001b
			Ouyang et al., 1998
	<i>Acanthopanax nipponicus</i> Makino	Triterpenoid	Miyakoshi et al., 1999
	<i>Aralia dasyphylla</i> Miq.	Triterpenoid	Xiao et al., 1999
	<i>Aralia elata</i> (Miq.) Seem.	Triterpenoid	Song et al., 2000, 2001
	<i>Cussonia bancoensis</i> Aubrev. & Pellegr.	Triterpenoid	Tapondjou et al., 2003
	<i>Cussonia racemosa</i> Baker	Triterpenoid	Harinantenaina et al., 2002
	<i>Hedera colchica</i> K.Koch	Triterpenoid	Delmas et al., 2000
			Mshvildadze et al., 2000, 2001
	<i>Hedera helix</i> L.	Triterpenoid	Barthomeuf et al., 2002
			Delmas et al., 2000
	<i>Kalopanax pictus</i> Nakai	Triterpenoid	Bedir et al., 2000
			Park et al., 2001
			Li et al., 2002
	<i>Meryta lanceolata</i> Forst.	Triterpenoid	Choi et al., 2002
	<i>Panax ginseng</i> C.A.Mey.	Triterpenoid	Melek et al., 2003
	<i>Panax japonicus</i> C.A.Mey.	Triterpenoid	Dou et al., 2001
	<i>Panax notoginseng</i> (Burk.) F.H.Chen	Triterpenoid	Zou et al., 2002a, 2002b
			Ma et al., 1999
	<i>Panax pseudo-ginseng</i> Wall.	Triterpenoid	Yoshikawa et al., 2001, 2003
	<i>Panax vietnamensis</i> Ha & Grushv.	Triterpenoid	Tanaka et al., 2000
			Huong et al., 1998b
	<i>Polyscias fruticosa</i> (L.) Harms [= <i>Panax fruticosum</i> L.; <i>Nothopanax fruticosum</i> Miq.]	Triterpenoid	Tran et al., 2001a, 2002
	<i>Schefflera leucantha</i> R.Vig.	Saponin mixture	Huan et al., 1998
	<i>Trevesia palmata</i> (Roxb. ex Lindl.) Vis.	Triterpenoid	Witthawaskul et al., 2003
	<i>Tupidanthus calyptratus</i> Hook.f. & Thoms.	Triterpenoid	De Tommasi et al., 2000
			Cioffi et al., 2001

Table 1 (Continued)

Family	Species	Saponin type	Reference
Chenopodiaceae	<i>Beta vulgaris</i> L.	Triterpenoid	Murakami et al., 1999a
	<i>Chenopodium album</i> L.	Triterpenoid	Lavaud et al., 2000
	<i>Chenopodium ficifolium</i> Sm.	Triterpenoid	Gohar et al., 2002
	<i>Chenopodium quinoa</i> Willd.	Triterpenoid	Dini et al., 2001a, 2001b
			Woldemichael and Wink, 2001 Dini et al., 2002 Zhu et al., 2002
Combretaceae	<i>Pteleopsis hylodendron</i> Mildbr.	Triterpenoid	Ngounou et al., 1999
Cucurbitaceae	<i>Cucurbita foetidissima</i> H.B. & K. [= <i>Cucurbita perrenis</i> A.Gray; <i>Cucumis perrenis</i> E.James]	Triterpenoid	Gaidi et al., 2000a
	<i>Cyclanthera pedata</i> Schrad.	Triterpenoid	De Tommasi et al., 1999
	<i>Momordica charantia</i> L.	Triterpenoid	Murakami et al., 2001a
Diapensiaceae	<i>Berneuxia tibetica</i> Decne.	Triterpenoid	Wang et al., 1998
Dioscoreaceae	<i>Dioscorea panthaica</i> Prain & Burkill	Steroidal	Dong et al., 2001a, 2001b
	<i>Dioscorea pseudojaponica</i> Yamamoto	Steroidal	Yang et al., 2003
Dipsacaceae	<i>Scabiosa rotata</i> M.Bieb.	Triterpenoid	Baykal et al., 1998
Dracaenaceae	<i>Dracaena angustifolia</i> Roxb.	Steroidal	Tran et al., 2001b
	<i>Dracaena concinna</i> Kunth	Steroidal	Mimaki et al., 1998e
	<i>Dracaena draco</i> L.	Steroidal	Mimaki et al., 1999c González et al., 2003
	<i>Dracaena surculosa</i> Lindl.	Steroidal	Yokosuka et al., 2000b, 2002a
	<i>Sansevieria cylindrica</i> Boj.	Steroidal	Antunes et al., 2003
Eupteleaceae	<i>Euptelea polyandra</i> Sieb. & Zucc.	Triterpenoid	Yoshikawa et al., 2000b Murakami et al., 2001b
Hippocastanaceae	<i>Aesculus chinensis</i> Bunge	Triterpenoid	Yang et al., 1999 Zhang et al., 1999a Zhao et al., 2001
Lamiaceae	<i>Becium grandiflorum</i> (Lam.) Pichi-Serm. var. <i>obovatum</i> (E.Mey. ex Benth) Sebald	Triterpenoid	Burger et al., 1998
Lardizabalaceae	<i>Holboellia fargesii</i> Reaub.	Triterpenoid	Fu et al., 2001
Lecythidaceae	<i>Barringtonia asiatica</i> Kurz	Triterpenoid	Herlt et al., 2002
	<i>Foetidia africana</i> Verdc.	Triterpenoid	Crublet et al., 2002
	<i>Petersianthus macrocarpus</i> (P.Beauv.) Liben	Triterpenoid	Olugbade et al., 2000
Leguminosae	<i>Acacia concinna</i> Wall.	Triterpenoid	Tezuka et al., 2000
	<i>Acacia tenuifolia</i> (L.) Willd.	Triterpenoid	Seo et al., 2002b
	<i>Acacia victoriae</i> Benth.	Triterpenoid	Hanausek et al., 2001

Table 1 (Continued)

Family	Species	Saponin type	Reference
	<i>Albizia gummifera</i> C.A.Sm.	Triterpenoid	Mujoo et al., 2001
	<i>Albizia julibrissin</i> Durazz.	Triterpenoid	Jayatilake et al., 2003
	<i>Albizia lebbeck</i> Willd.	Saponin mixture	Debella et al., 2000
	<i>Albizia myriophylla</i> Benth.	Triterpenoid	Zou et al., 2000
	<i>Albizia procera</i> Benth.	Triterpenoid	Une et al., 2001
	<i>Albizia subdimidiata</i> (Splitg.)	Triterpenoid	Yoshikawa et al., 2002
	Barneby & J.W.Grimes		Yoshikawa et al., 1998
	<i>Astragalus kahiricus</i> DC.	Triterpenoid	Abdel-Kader et al., 2001
	<i>Astragalus trigonus</i> DC.	Triterpenoid	Verotta et al., 2002
	<i>Baptisia australis</i> (L.) R.Br.	Triterpenoid	Shaker et al., 2001
	<i>Gleditsia sinensis</i> Lam.	Triterpenoid	Udayama et al., 1998
	<i>Gliricidia sepium</i> (Jacq.) Walp.	Triterpenoid	Zhang et al., 1999b, 1999c, 1999d
	<i>Gliricidia sepium</i> (Jacq.) Steud.		Kojima et al., 1998
	<i>Lathyrus japonicus</i> Willd. [= <i>Lathyrus maritimus</i> Bigel.]	Triterpenoid	Rastrelli et al., 1999
	<i>Lupinus oreophilus</i> Phil.	Triterpenoid	Kang et al., 1998
	<i>Medicago sativa</i> L.	Triterpenoid	Woldemichael et al., 2003
	<i>Spartium junceum</i> L.	Triterpenoid	Bialy et al., 1999
	<i>Swartzia schomburgkii</i> Benth.	Triterpenoid	Yeşilada and Takaishi, 1999
	var. <i>schomburgkii</i>		Abdel-Kader et al., 2000
	<i>Trifolium</i> spp.	Triterpenoid	
	<i>Trifolium resupinatum</i> L.	Triterpenoid	Oleszek and Stochmal, 2002
	<i>Trigonella foenum-graecum</i> L.	Steroidal	Simonet et al., 1999
	<i>Vigna angularis</i> (Willd.) Ohwi & H. Ohashi	Triterpenoid	Murakami et al., 2000a
Liliaceae	<i>Camassia leichlinii</i> (Bak.) S.Wats.	Steroidal	Iida et al., 1999
	<i>Chlorophytum malayense</i> Ridl.	Steroidal	Kuroda et al., 2001
	<i>Hemerocallis fulva</i> L. var. <i>kwanso</i>	Steroidal	Qiu et al., 2000
	<i>Hosta sieboldii</i> (Paxton) I.Ingram	Steroidal	Konishi et al., 2001
	<i>Lilium candidum</i> L.	Steroidal	Mimaki et al., 1998c
	<i>Polygonatum zanzlancianense</i> Pamp.	Steroidal	Haladova et al., 1998
	<i>Ruscus aculeatus</i> L.	Steroidal	Mimaki et al., 1999e
	<i>Ruscus colchicus</i> Yeo	Steroidal	Wang et al., 2001
	<i>Ruscus hypoglossum</i> L.	Steroidal	Mimaki et al., 1998a, 1998b, 1999d
	<i>Tupistra wattii</i> Hook.f.	Steroidal	de Combarieu et al., 2002
Lythraceae	<i>Lafoensia glyptocarpa</i> Koehne	Triterpenoid	de Combarieu et al., 2002
Menispermaceae	<i>Diploclostia glaucescens</i> (Bl.) Diels [= <i>Cocculus macrocarpus</i> Wight & Arn.]	Triterpenoid	Shen et al., 2003
Molluginaceae	<i>Glinus lotoides</i> L. var. <i>dictamnoides</i> [= <i>Glinus dictamnoides</i> Burm.f.; <i>Mollugo glinus</i> A.Rich]	Triterpenoid	de Carvalho et al., 1999
	<i>Glinus oppositifolius</i> L.	Triterpenoid	Jayasinghe et al., 2003
	<i>Mollugo spargula</i> L.	Triterpenoid	Hamed and El-Emary, 1999
		Triterpenoid	Traore et al., 2000
		Triterpenoid	Sahu et al., 2001

Table 1 (Continued)

Family	Species	Saponin type	Reference
Myrsinaceae	<i>Ardisia crenata</i> Roxb.	Triterpenoid	Koike et al., 1999b
	<i>Ardisia mamillata</i> Hance	Triterpenoid	Huang et al., 2000a, 2000b
	<i>Maesa japonica</i> (Thunb.) Mor. & Zoll.	Triterpenoid	Koike et al., 1999c
	<i>Maesa lanceolata</i> Forssk. var. <i>golungensis</i> Welw.	Triterpenoid	Sindambiwe et al., 1998 Apers et al., 1999, 2001
	<i>Maesa laxiflora</i> Pitard	Triterpenoid	Jiang et al., 1999
	<i>Maesa tenera</i> Mez	Triterpenoid	Koike et al., 2001
Passifloraceae	<i>Passiflora edulis</i> Sims	Triterpenoid	Yoshikawa et al., 2000a
Phytolaccaceae	<i>Phytolacca dioica</i> L.	Triterpenoid	Soliman et al., 2001
	<i>Phytolacca dodecandra</i> L'Hér.	Saponin mixture	Mølgaard et al., 2000
	<i>Phytolacca icosandra</i> L.	Triterpenoid	Treyvaud et al., 2000
	<i>Phytolacca tetramera</i> Hauman	Triterpenoid	Escalante et al., 2002
Pittosporaceae	<i>Pittosporum viridiflorum</i> Sims	Triterpenoid	Seo et al., 2002a
Polygalaceae	<i>Carpolobia alba</i> G.Don.	Triterpenoid	Mitaine-Offer et al., 2002
	<i>Carpolobia lutea</i> G.Don.	Triterpenoid	Mitaine-Offer et al., 2002
	<i>Polygala amarella</i> Crantz	Triterpenoid	Desbène et al., 1999
	<i>Polygala senega</i> L.	Triterpenoid	Estrada et al., 2000
	<i>Securidaca</i> <i>inappendiculata</i> Hassk.	Triterpenoid	Yui et al., 2001
Primulaceae	<i>Cyclamen coum</i> mill.	Triterpenoid	Yayli et al., 1998
Ranunculaceae	<i>Cimicifuga foetida</i> L.	Triterpenoid	Zhu et al., 2001
	<i>Clematis tangutica</i> (Maxim.) Korsh.	Triterpenoid	Zhong et al., 2001
	<i>Clematis tibetana</i> Kuntze	Triterpenoid	Kawata et al., 2001
	<i>Eranthis cilicica</i> Schott & Kotschy	Triterpenoid	Watanabe et al., 2003
	<i>Nigella sativa</i> L.	Triterpenoid	Kumara and Huat, 2001
	<i>Pulsatilla chinensis</i> (Bunge) Regel	Triterpenoid	Mimaki et al., 1999a
	<i>Pulsatilla patens</i> Mill var. <i>multifida</i> (Pritz.) S.H.Li & Y.H.Huang	Triterpenoid	Ye et al., 1999
	<i>Thalictrum minus</i> L.	Triterpenoid	Gromova et al., 1998
	<i>Colubrina retusa</i> L.	Triterpenoid	ElSohly et al., 1999 Li et al., 1999b
	<i>Zizyphus joazeiro</i> Mart. <i>Zizyphus jujuba</i> Mill. var. <i>spinosa</i> Hu.	Triterpenoid Triterpenoid	Schühly and Heilmann, 2000 Matsuda et al., 1999
Rosaceae	<i>Quillaja saponaria</i> Molina	Triterpenoid	Guo et al., 1998, 2000 Guo and Kenne, 2000a, 2000b Marciani et al., 2001 Wang et al., 2000
	<i>Rubus pungens</i> Camb. var. <i>oldhamii</i> Maxim.	Triterpenoid	
Rubiaceae	<i>Galium rivale</i> (Sibth. & Sm.) Griseb.	Triterpenoid	de Rosa et al., 2000a, 2000b
	<i>Hedyotis nudicaulis</i> Wight & Arn.	Triterpenoid	Konishi et al., 1998
	<i>Isertia pittieri</i> (Standl.) Standl.	Triterpenoid	Um et al., 2001
	<i>Randia formosa</i> K.Schum.	Triterpenoid	Sahpaz et al., 2000
	<i>Rudgea viburnoides</i> (Cham.) Benth.	Triterpenoid	Young et al., 1998

Table 1 (Continued)

Family	Species	Saponin type	Reference
Sapindaceae	<i>Elattostachys apetala</i> (Labill.) Radlk. [= <i>Elattostachys falcata</i> (A. Gray) Radlk.]	Triterpenoid	Lavaud et al., 2001
	<i>Filicium decipiens</i> Thwaites	Triterpenoid	Lavaud et al., 1998
	<i>Harpullia austro-caledonica</i> Boull.	Triterpenoid	Voutquenne et al., 2002
	<i>Harpullia cupanioides</i> Roxb.	Triterpenoid	Voutquenne et al., 1998
	<i>Harpulia ramiflora</i> Radlk.	Triterpenoid	Dizes et al., 1998
	<i>Koelreuteria paniculata</i> Laxm.	Triterpenoid	Soliman et al., 2001
	<i>Pometia ridleyi</i> King emend. Radlk.	Triterpenoid	Voutquenne et al., 2003
	<i>Sapindus emarginatus</i> Vahl.	Triterpenoid	Kanchanapoom et al., 2001
	<i>Sapindus mukorossi</i> Gaertn.	Triterpenoid	Huang et al., 2003
Sapotaceae	<i>Argania spinosa</i> (L.) Skeels	Triterpenoid	Alaoui et al., 2002
	<i>Gambeya boukokoensis</i> Aubrev. & Pellegr.	Triterpenoid	Wandji et al., 2003
	<i>Madhuca longifolia</i> (L.) Macbride [= <i>Bassia longifolia</i> L.]	Triterpenoid	Yoshikawa et al., 2000c
	<i>Tieghemella heckelii</i> Pierre ex A.Chev.	Triterpenoid	Gosse et al., 2002
Scrophulariaceae	<i>Bacopa monniera</i> Wettst.	Triterpenoid	Pawar et al., 2001
Solanaceae	<i>Capsicum annuum</i> L. var. <i>acuminatum</i> Fingerh.	Steroidal	Iorizzi et al., 2002
	<i>Capsicum frutescens</i> L.	Steroidal	de Lucca et al., 2002
	<i>Cestrum nocturnum</i> L.	Steroidal	Mimaki et al., 2001a
	<i>Cestrum sendmerianum</i> Mart. Ex Sendt.	Steroidal	Haraguchi et al., 1999, 2000
	<i>Lycopersicon esculentum</i> Mill.	Steroidal	Fujiwara et al., 2003
	<i>Solanum chrysotrichum</i> Schldh.	Steroidal	Alvarez et al., 2001
	<i>Solanum khasianum</i> C.B. Clarke	Steroidal	Zamilpa et al., 2002 Putalun et al., 1999
Styracaceae	<i>Styrax officinalis</i> L.	Triterpenoid	Yayla et al., 2002
Taccaceae	<i>Tacca chantrieri</i> André	Steroidal	Yokosuka et al., 2002b
Ternstroemiaceae	<i>Camellia sinensis</i> L. var. <i>assamica</i> Pierre	Triterpenoid	Murakami et al., 1999b, 2000b Lu et al., 2000
	<i>Ternstroemia japonica</i> Thunb.	Triterpenoid	Shin et al., 2003
Tiliaceae	<i>Corchorus depressus</i> L.	Triterpenoid	Ahmad et al., 2000
Verbenaceae	<i>Duranta repens</i> L.	Triterpenoid	Hiradate et al., 1999
Zygophyllaceae	<i>Fagonia cretica</i> L.	Triterpenoid	Khalik et al., 2000
	<i>Fagonia indica</i> Burm.f.	Triterpenoid	Shaker et al., 1999
	<i>Tribulus terrestris</i> L.	Steroidal	Xu et al., 2000 Cai et al., 2001 Kostova et al., 2002 de Combarieu et al., 2003 Pöllmann et al., 1998
	<i>Zygophyllum decumbens</i> Del.	Triterpenoid	
	<i>Zygophyllum gaetulum</i> Emb. & Maire	Triterpenoid	Safir and Fkih-Tetouani, 1998
			Aquino et al., 2001

the typical response in cancer cells, were isolated from the root bark of *Becium grandiflorum* (Lam.) Pichi-Serm. var. *obovatum* (E.Mey. ex Benth) Sebald (Lamiaceae) due to the traditional use of the plant (along with four others) for the treatment of breast and buccal cancer (Burger et al., 1998). A further 10% of the species listed were selected based on previous ethnobotanical studies on related species either of the same genus or family. *Allium nutans* L. (Alliaceae), a wild species of onion, was investigated because of the many reports on the steroidal saponins from *Allium* species (Akhov et al., 1999). This approach to drug discovery has received renewed interest in recent years, and potentially increases the chances for the discovery of novel therapeutic agents (Fabricant and Farnsworth, 2001).

As mentioned earlier, steroidal saponins are almost exclusively found in the monocotyledonous angiosperms. This trend is confirmed by the presence of steroidal saponins in the monocotyledonous families of the Agavaceae, Alliaceae, Asparagaceae, Dioscoreaceae, Dracaenaceae, Liliaceae and Taccaceae. Interestingly, although the family Solanaceae is dicotyledonous, all the species studied contained steroidal saponins. Other exceptions include the presence of steroidal saponins in *Aspilia montevidensis* (Asteraceae), *Balanites aegyptiaca* (Balanitaceae), *Trigonella foenum-graecum* (Leguminosae) and *Tribulus terrestris* (Zygophyllaceae).

Eighteen species of the family Araliaceae have been extensively investigated, as seen in Table 1, five of which are from the genus *Panax*. Species of *Panax* (ginseng) have been known to contain saponins for centuries, however, recent studies on ginseng saponins have investigated their biological activities (Huong et al., 1998b; Kim et al., 1998b; Kim and Kim, 1999; Tran et al., 2001a, 2002; Liao et al., 2002; Zou et al., 2002a; Yoshikawa et al., 2003). The Leguminosae have also been extensively investigated for saponins, in particular, species of *Acacia*, *Albizia* and *Astragalus*. Table 1 lists 23 species of the Leguminosae from which saponins have been isolated.

4. Conclusion

Saponins are a diverse family of secondary metabolites produced by many plants species. Many plants used in traditional medicine worldwide contain saponins, which can often account for their therapeutic action. It is believed that the natural role of these compounds in plants is to protect against attack by potential pathogens, which would account for their antimicrobial activity (Osbourne, 2003). Although saponins are extremely toxic to cold-blooded animals, their oral toxicity to mammals is low (Dini et al., 2001a, 2001b). Due to their toxicity to various organisms, saponins can be utilised for their insecticidal, antibiotic, fungicidal, and pharmacological properties. The wide chemical diversity of both triterpenoid and steroidal saponins has resulted in renewed interest and investigations of these compounds in recent years, particularly as potential chemotherapeutic agents.

This review, and the list of species presented in Table 1, provides a summary of saponin research in the last 5 years. It highlights important areas of research in this field, and the opportunity which exists for further research on the phytochemistry and biological activity of this group of compounds. Balandrin et al. (1993) estimate that at least 85% of the world's estimated 250 000 species of higher plants have not been adequately surveyed for potentially useful biological activity. As a result, the chances of discovering new plant constituents, including novel saponins, which may be biologically active are promising.

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References

- Abdel-Gawad, M.M., El-Sayed, M.M., Abdel-Hameed, E.S., 1999. Molluscicidal steroidal saponins and lipid content of *Agave decipiens*. *Fittoterapia* 70, 371–381.
- Abdel-Kader, M.S., Bahler, B.D., Malone, S., Werkhoven, M.C.M., Wisse, J.H., Neddermann, K.M., Bursuker, I., Kingston, D.G.I., 2000. Bioactive saponins from *Swartzia schomburgkii* from the Suriname rainforest. *Journal of Natural Products* 63, 1461–1464.
- Abdel-Kader, M., Hoch, J., Berger, J.M., Evans, R., Miller, J.S., Wisse, J.H., Mamber, S.W., Dalton, J.M., Kingston, D.G.I., 2001. Two bioactive saponins from *Albizia subdimidiata* from the Suriname rainforest. *Journal of Natural Products* 64, 536–539.
- Acebes, B., Bernabé, M., Díaz-Lanza, A.M., Bartolomé, C., 1998a. Two new sulfated saponins from the roots of *Gypsophila bermejoi*. *Journal of Natural Products* 61, 1557–1559.
- Acebes, B., Díaz-Lanza, A.M., Bernabé, M., 1998b. A saponin from the roots of *Gypsophila bermejoi*. *Phytochemistry* 49, 2077–2079.
- Ahmad, V.U., Khaliq-uz-Zaman, S.M., Shameel, S., Perveen, S., Ali, Z., 1998. Steroidal saponins from *Asparagus dumosus*. *Phytochemistry* 50, 481–484.
- Ahmad, V.U., Ali, A., Ali, Z., Zafar, F.N., Zahid, M., 2000. Novel cycloartane saponins from *Corchorus depressus* L. *Chemical and Pharmaceutical Bulletin* 48, 1591–1601.
- Ahn, B.-Z., Yoon, Y.-D., Lee, Y.H., Kim, B.-H., Sok, D.-E., 1998. Inhibitory effect of bupleuri radix saponins on adhesion of some solid tumor cells and relation to hemolytic action: Screening of 232 herbal drugs for anti-cell adhesion. *Planta Medica* 64, 220–224.
- Akhov, L.S., Musienko, M.M., Piacente, S., Pizzi, C., Oleszek, W., 1999. Structure of steroidal saponins from underground parts of *Allium nutans* L. *Journal of Agricultural and Food Chemistry* 47, 3193–3196.
- Alaoui, A., Charrouf, Z., Soufiaoui, M., Carbone, V., Malorni, A., Pizzi, C., Piacente, S., 2002. Triterpenoid saponins from the shells of *Argania spinosa* seeds. *Journal of Agricultural and Food Chemistry* 50, 4600–4603.
- Alvarez, L., Pérez, M.D.C., González, J.L., Navarro, V., Villarreal, M.L., Olson, J.O., 2001. SC-1, an antimycotic spirostan saponin from *Solanum chrysotrichum*. *Planta Medica* 67, 372–374.
- Antunes, A.D., da Silva, B.P., Parente, J.P., Valente, A.P., 2003. A new bioactive steroidal saponin from *Sansevieria cylindrica*. *Phytotherapy Research* 17, 179–182.
- Apers, S., De Bruyne, T.E., Claeys, M., Vlietinck, A.J., Pieters, L.A.C., 1999. New acylated triterpenoid saponins from *Maesa lanceolata*. *Phytochemistry* 52, 1121–1131.

- Apers, S., Varonikova, S., Sindambiwe, J.-B., Witvrouw, M., De Clercq, E., Vanden Berghe, D., Van Marck, E., Vlietinck, A., Pieters, L., 2001. Antiviral, haemolytic and molluscicidal activities of triterpenoid saponins from *Maesa lanceolata*: establishment of structure–activity relationships. *Planta Medica* 67, 528–532.
- Aquino, R., Tortora, S., Rkih-Tetouani, S., Capasso, A., 2001. Saponins from the roots of *Zygophyllum gaetulum* and their effects on electrically-stimulated guinea-pig ileum. *Phytochemistry* 56, 393–398.
- Atta-ur-Rahman, Shahwar, D., Choudhary, M.I., Sener, B., Toker, G., Baser, K.H.C., 2000. Triterpenoid saponins from *Bongardia chrysogonum*. *Journal of Natural Products* 63, 251–253.
- Attele, S.A., Wu, J.A., Yuan, C.-S., 1999. Ginseng pharmacology, multiple constituents and multiple actions. *Biochemical Pharmacology* 58, 1685–1693.
- Avila, J.G., Romo de Vivar, A., 2002. Triterpenoid saponins and other glycosides from *Buddleja scordioides*. *Biochemical Systematics and Ecology* 30, 1003–1005.
- Baba, M., Ohmura, M., Kishi, N., Okada, Y., Shibata, S., Peng, J., Yao, S.-S., Nishino, H., Okuyama, T., 2000. Saponins isolated from *Allium chinense* G. Don and antitumor-promoting activities of isoliquiritigenin and laxogenin from the same drug. *Biological and Pharmaceutical Bulletin* 23, 660–662.
- Bader, G., Seibold, M., Tintelnot, K., Hiller, K., 2000. Cytotoxicity of triterpenoid saponins. Part 2. Relationships between the structures of glycosides of polygalic acid and their activities against pathogenic *Candida* species. *Pharmazie* 55, 72–74.
- Balandrin, M.F., Kinghorn, A.D., Farnsworth, N.R., 1993. Plant-derived natural products in drug discovery and development. In: Kinghorn, A.D., Balandrin, M.F. (Eds.), *Human Medicinal Agents from Plants*. ACS Symposium Series 534. American Chemical Society, Washington, DC, pp. 2–12.
- Barr, I.G., Sjölander, A., Cox, J.C., 1998. Iscoms and other saponin based adjuvants. *Advanced Drug Delivery Reviews* 32, 247–271.
- Barthomeuf, C., Debiton, E., Mshvildadze, V., Kemertelidze, E., Balansard, G., 2002. In vitro activity of hederacolchisid A₁ compared with other saponins from *Hedera colchica* against proliferation of human carcinoma and melanoma cells. *Planta Medica* 68, 672–675.
- Baumann, E., Stoya, G., Völkner, A., Richter, W., Lemke, C., Linss, W., 2000. Hemolysis of human erythrocytes with saponin affects the membrane structure. *Acta Histochemica* 102, 21–35.
- Baykal, T., Panayir, T., Tasdemir, D., Sticher, O., Çalis, I., 1998. Triterpene saponins from *Scabiosa rotata*. *Phytochemistry* 48, 867–873.
- Bedir, E., Kirmizipekmez, H., Sticher, O., Çalis, I., 2000. Triterpene saponins from the fruits of *Hedera helix*. *Phytochemistry* 53, 905–909.
- Bellini, A.A., Camilo, D., De Oliveira, R., Vichnewski, W., 1999. Steroidal saponin, 7-oxostigmasterol and diterpenes from *Aspilia montevidensis*. *Biochemical Systematics and Ecology* 27, 317–319.
- Berhow, M.A., Wagner, E.D., Vaughn, S.F., Plewa, M.J., 2000. Characterization and antimutagenic activity of soybean saponins. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis* 448, 11–22.
- Bialy, Z., Jurzysta, M., Oleszek, W., Piacente, S., Pizza, C., 1999. Saponins in alfalfa (*Medicago sativa* L.) root and their structural elucidation. *Journal of Agricultural and Food Chemistry* 47, 3185–3192.
- Bruneton, J., 1995. *Pharmacognosy, Phytochemistry, Medicinal Plants*. Lavoisier Publishing, Paris, pp. 538–544 (ISBN 2-4730-0028-7).
- Burger, I., Burger, B.V., Albrecht, C.F., Spies, H.S.C., Sándor, P., 1998. Triterpenoid saponins from *Becium grandiflorum* var. *obovatum*. *Phytochemistry* 49, 2087–2095.
- Cai, L., Wu, Y., Zhang, J., Pei, F., Xu, Y., Xie, S., Xu, D., 2001. Steroidal saponins from *Tribulus terrestris*. *Planta Medica* 67, 196–198.
- Carotenuto, A., Fattorusso, E., Lanzotti, V., Magno, S., 1999. Spirostanol saponins of *Allium porrum* L. *Phytochemistry* 51, 1077–1082.
- Corea, G., Fattorusso, E., Lanzotti, 2003. Saponins and flavonoids of *Allium triquetrum*. *Journal of Natural Products* 66, 1405–1411.
- Choi, J., Huh, K., Kim, S.-H., Lee, K.-T., Park, H.-J., Han, Y.N., 2002. Antinociceptive and anti-rheumatoid effects of *Kalopanax pictum* extract and its saponin components in experimental animals. *Journal of Ethnopharmacology* 79, 199–204.
- Cioffi, G., Bellino, A., Pizza, C., Venturella, F., De Tommasi, N., 2001. Triterpene saponins from *Tupidanthus calyptratus*. *Journal of Natural Products* 64, 750–753.
- Crublet, M.-L., Pouny, I., Delaude, C., Lavaud, C., 2002. Acylated triterpenoid saponins from the stem bark of *Foetidia africana*. *Journal of Natural Products* 65, 1560–1567.
- da Silva, B.P., De Sousa, A.C., Silva, G.M., Mendes, T.P., Parente, J.P., 2002. A new bioactive steroidal saponin from *Agave attenuata*. *Zeitschrift für Naturforschung C* 57, 423–428.
- de Andrade, F.D.P., Piacente, S., Pizza, C., Vilegas, W., 2002. Studies on the constituents of a Brazilian folk infusion. Isolation and structure elucidation of new triterpene saponins from *Ilex amara* leaves. *Journal of Agricultural and Food Chemistry* 50, 255–261.
- de Carvalho, G.J.A., De Carvalho, M.G., Braz-Filho, R., 1999. A triterpenoid saponin isolated from *Lafoensia glyptocarpa*. *Phytochemistry* 52, 1617–1619.
- de Combarieu, E., Falzoni, M., Fuzzati, N., Gattesco, F., Giori, A., Lovati, M., Pace, R., 2002. Identification of *Ruscus* steroidal saponins by HPLC-MS analysis. *Fitoterapia* 73, 583–596.
- de Combarieu, E., Fuzzati, N., Lovati, M., Mercalli, E., 2003. Furostanol saponins from *Tribulus terrestris*. *Fitoterapia* 74, 583–591.
- de Lucca, A., Bland, J.M., Vigo, C.B., Cushion, M., Selitrennikoff, C.P., Peter, J., Walsh, T.J., 2002. CAY-1, a fungicidal saponin from *Capsicum* sp. fruit. *Medical Mycology* 40, 131–137.
- de Rosa, S., Iodice, C., Mitova, M., Handjieva, N., Popov, S., Anchev, M., 2000a. Triterpene saponins and iridoid glucosides from *Galium rivale*. *Phytochemistry* 54, 751–756.
- de Rosa, S., Mitova, M., Handjieva, N., Popov, S., Anchev, M., 2000b. Rivalosides A and B, two 19-oxo triterpenoid saponins from *Galium rivale*. *Journal of Natural Products* 63, 1012–1014.
- De Tommasi, N., Piacente, S., Gacs-Baitz, E., De Simone, F., Pizza, C., Aquino, R., 1998. Triterpenoid saponins from *Spergularia ramosa*. *Journal of Natural Products* 61, 323–327.
- De Tommasi, N., De Simone, F., Speranza, G., Pizza, C., 1999. Studies on the constituents of *Cyclanthera pedata* fruits: isolation and structure elucidation of new triterpenoid saponins. *Journal of Agricultural and Food Chemistry* 47, 4512–4519.
- De Tommasi, N., Autore, G., Bellino, A., Pinto, A., Pizza, C., Sorrentino, R., Venturella, P., 2000. Antiproliferative triterpene saponins from *Trevesia palmata*. *Journal of Natural Products* 63, 308–314.
- Debella, A., Haslinger, E., Kunert, O., Michl, G., Abebe, D., 1999. Steroidal saponins from *Asparagus africanus*. *Phytochemistry* 51, 1069–1075.
- Debella, A., Haslinger, E., Schmid, M.G., Bucar, F., Michl, G., Abebe, D., Kunert, O., 2000. Triterpenoid saponins and saponin lactones from *Albizia gummifera*. *Phytochemistry* 53, 885–892.
- Delmas, F., Di Giorgio, C., Elias, R., Gasquet, M., Azas, Mshvildadze, V., Dekanosidze, G., Kemertelidze, E., Timon-David, P., 2000. Antileishmanial activity of three saponins isolated from ivy, α -hederin, β -hederin and hederacolchiside A₁, as compared to their action on mammalian cells cultured in vitro. *Planta Medica* 66, 343–347.
- Desbène, S., Hanquet, B., Shoyama, Y., Wagner, H., Lacaille-Dubois, M.-A., 1999. Biologically active triterpene saponins from callus tissue of *Polygala amarella*. *Journal of Natural Products* 62, 923–926.
- Dini, I., Schettino, O., Simioli, T., Dini, A., 2001a. Studies on the constituents of *Chenopodium quinoa* seeds: isolation and characterization of new triterpene saponins. *Journal of Agricultural and Food Chemistry* 49, 741–746.
- Dini, I., Tenore, G.C., Schettino, O., Dini, A., 2001b. New oleanane saponins in *Chenopodium quinoa*. *Journal of Agricultural and Food Chemistry* 49, 3976–3981.
- Dini, I., Tenore, G.C., Dini, A., 2002. Oleanane saponins in “kancolla”, a sweet variety of *Chenopodium quinoa*. *Journal of Natural Products* 65, 1023–1026.

- Dizes, C., Gerald, F., Lavaud, C., Elias, R., Faure, R., Massiot, G., Balansard, G., 1998. Harpuloside A triterpenoid saponins from *Harpullia ramiflora*. *Phytochemistry* 48, 1229–1232.
- Dong, M., Feng, X.-Z., Wang, B.-X., Wu, L.-J., Ikejima, T., 2001a. Two novel furostanol saponins from the rhizomes of *Dioscorea panthaica* Prain et Burkill and their cytotoxic activity. *Tetrahedron* 57, 501–506.
- Dong, M., Feng, X.-Z., Wu, L.-J., Wang, B.-X., Ikejima, T., 2001b. Two new steroidal saponins from the rhizomes of *Dioscorea panthaica* and their cytotoxic activity. *Planta Medica* 67, 853–857.
- Dou, D.-Q., Chen, Y.-J., Liang, L.-H., Pang, F.-G., Shimizu, N., Takeda, T., 2001. Six new dammarane-type triterpene saponins from the leaves of *Panax ginseng*. *Chemical and Pharmaceutical Bulletin* 49, 442–446.
- Elgamal, M.H.A., Soliman, H.S.M., Elmunajjed, D.T., Tóth, G., Simon, A., Duddeck, H., 1998. Two triterpene saponins from *Arenaria filiculis*. *Phytochemistry* 49, 189–193.
- ElSohly, H.N., Danner, S., Li, X.-C., Nimrod, A.C., Clark, A.M., 1999. New antimycobacterial saponin from *Colubrina retusa*. *Journal of Natural Products* 62, 1341–1342.
- Escalante, A.M., Santecchia, C.B., López, S.N., Gattuso, M.A., Ravelo, A.G., Monache, F.D., Sierra, M.G., Zacchino, S.A., 2002. Isolation of antifungal saponins from *Phytolacca tetramera*, an Argentinean species in critic risk. *Journal of Ethnopharmacology* 82, 29–34.
- Estrada, A., Katselis, G.S., Laarveld, B., Barl, B., 2000. Isolation and evaluation of immunological adjuvant activities of saponins from *Polygala senega* L. *Comparative Immunology, Microbiology and Infectious Diseases* 23, 27–43.
- Fabricant, D.S., Farnsworth, N.R., 2001. The value of plants used in traditional medicine for drug discovery. *Environmental Health Perspectives* 109, 69–75.
- Fattorusso, E., Lanzotti, V., Tagliatela-Scafati, O., Di Rosa, M., Ianaro, A., 2000. Cytotoxic saponins from bulbs of *Allium porrum* L. *Journal of Agricultural and Food Chemistry* 48, 3455–3462.
- Fu, H., Koike, K., Zheng, Q., Mitsunaga, K., Jia, Z., Nikaido, T., Lin, W., Guo, D., Zhang, L., 2001. Fargosides A-E, triterpenoid saponins from *Holboellia fargesii*. *Chemical and Pharmaceutical Bulletin* 49, 999–1002.
- Fujioka, T., Yoshida, K., Jujii, H., Nagao, T., Okabe, H., Mihashi, K., 2003. Antiproliferative constituents from Umbelliferae plants VI. New ursane-type saikosaponin analogs from the fruits of *Bupleurum rotundifolium*. *Chemical and Pharmaceutical Bulletin* 51, 365–372.
- Fujiwara, Y., Yahara, S., Ikeda, T., Ono, M., Nohara, T., 2003. Cytotoxic major saponin from tomato fruits. *Chemical and Pharmaceutical Bulletin* 51, 234–235.
- Fukuda, N., Tanaka, H., Shoyama, Y., 2000. Isolation of the pharmacologically active saponin Ginsenoside Rb1 from ginseng by immunoaffinity column chromatography. *Journal of Natural Products* 63, 283–285.
- Gaidi, G., Marouf, A., Hanquet, B., Bauer, R., Correia, M., Chauffert, B., Lacaille-Dubois, M.-A., 2000a. A new major triterpene saponin from the roots of *Cucurbita foetidissima*. *Journal of Natural Products* 63, 122–124.
- Gaidi, G., Miyamoto, T., Rustaiyan, A., Laurens, V., Lacaille-Dubois, M.-A., 2000b. Two new biologically active triterpene saponins from *Acanthophyllum squarrosum*. *Journal of Natural Products* 63, 1497–1502.
- Gaidi, G., Miyamoto, T., Lacaille-Dubois, M.-A., 2001a. Junceosides A–C, new triterpene saponins from *Arenaria juncea*. *Journal of Natural Products* 64, 1533–1537.
- Gaidi, G., Miyamoto, T., Rustaiyan, A., Lacaille-Dubois, M.-A., 2001b. Three new acylated triterpene saponins from *Acanthophyllum squarrosum*. *Journal of Natural Products* 64, 920–924.
- Gaidi, G., Miyamoto, T., Laurens, V., Lacaille-Dubois, M.-A., 2002. New acylated triterpene saponins from *Silene fortunei* that modulate lymphocyte proliferation. *Journal of Natural Products* 65, 1568–1572.
- Glensk, M., Wray, V., Nimtz, M., Schöpke, T., 1999. Silenosides A–C, triterpenoid saponins from *Silene vulgaris*. *Journal of Natural Products* 62, 717–721.
- Gohar, A.A., Maatooq, G.T., Niwa, M., Yoshiaki, T., 2002. A new triterpene saponin from *Chenopodium ficifolium*. *Zeitschrift für Naturforschung C* 57, 597–602.
- González, A.G., Hernández, J.C., León, F., Padrón, J.I., Estévez, F., Quintana, J., Bermejo, J., 2003. Steroidal saponins from the bark of *Dracaena draco* and their cytotoxic activities. *Journal of Natural Products* 66, 793–798.
- Gosse, B., Gnabre, J., Bates, R.B., Dicus, C.W., Nakkiew, P., Huang, R.C.C., 2002. Antiviral saponins from *Tieghemella heckelii*. *Journal of Natural Products* 65, 1942–1944.
- Gromova, A.S., Lutsky, V.I., Semenov, A.A., Li, D., Owen, N.L., 1998. The elucidation of the structure of thaliccoside F, a minor oleanane glycoside from *Thalictrum minus* L. *Phytochemistry* 47, 437–440.
- Guo, S., Kenne, L., Lundgren, L.N., Rönnerberg, B., Sundquist, B.G., 1998. Triterpenoid saponins from *Quillaja saponaria*. *Phytochemistry* 48, 175–180.
- Guo, S., Falk, E., Kenne, L., Rönnerberg, B., Sundquist, B.G., 2000. Triterpenoid saponins containing an acetylated branched D-fucosyl residue from *Quillaja saponaria* Molina. *Phytochemistry* 53, 861–868.
- Guo, S., Kenne, L., 2000a. Characterization of some O-acetylated saponins from *Quillaja saponaria* Molina. *Phytochemistry* 54, 615–623.
- Guo, S., Kenne, L., 2000b. Structural studies of triterpenoid saponins with new acyl components from *Quillaja saponaria* Molina. *Phytochemistry* 55, 419–428.
- Haladova, M., Eisenreichova, E., Mucaji, P., Budesinsky, M., Ubik, K., 1998. Steroidal saponins from *Lilium candidum* L. *Collection of Czechoslovak Chemical Communications* 63, 205–210.
- Hamed, A.I., El-Emary, N.A., 1999. Triterpene saponins from *Glinus lotoides* var. *dictamnoides*. *Phytochemistry* 50, 477–480.
- Hanausek, M., Ganesh, P., Walaszek, Z., Arntzen, C.J., Slaga, T.J., Gutternam, J.U., 2001. Avicins, a family of triterpenoid saponins from *Acacia victoriae* (Benth.), suppress H-ras mutations and aneuploidy in a murine skin carcinogenesis model. *Proceedings of the National Academy of Sciences USA* 98, 11551–11556.
- Haraguchi, M., Motidome, M., Morita, H., Takeya, K., Itokawa, H., Mimaki, Y., Sashida, Y., 1999. New polyhydroxylated steroidal sapogenin and saponin from the leaves of *Cestrum sendtnerianum*. *Chemical and Pharmaceutical Bulletin* 47, 582–584.
- Haraguchi, M., Mimaki, Y., Motidome, M., Morita, H., Takeya, K., Itokawa, H., Yokosuka, A., Sashida, Y., 2000. Steroidal saponins from the leaves of *Cestrum sendtnerianum*. *Phytochemistry* 55, 715–720.
- Haralampidis, K., Trojanowska, M., Osbourn, A.E., 2002. Biosynthesis of triterpenoid saponins in plants. *Advances in Biochemical Engineering/Biotechnology* 75, 31–49.
- Harinantenaina, L., Kasai, R., Yamasaki, K., 2002. Cussosaponins A–E, triterpene saponins from the leaves of *Cussonia racemosa*, a Malagasy endemic plant. *Chemical and Pharmaceutical Bulletin* 50, 1290–1293.
- Hayashi, K., Sagesaka, Y.M., Suzuki, T., Suzuki, Y., 1999. Inactivation of human type A and B influenza viruses by tea-seed saponins. *Bioscience Biotechnology and Biochemistry* 63, 184–186.
- Herlt, A.J., Mander, L.N., Pongoh, E., Rumampuk, R.J., Tarigan, P., 2002. Two major saponins from seeds of *Barringtonia asiatica*: putative antifedants toward *Epilachna* sp. larvae. *Journal of Natural Products* 65, 115–120.
- Hiradate, S., Yada, H., Ishii, T., Nakajima, N., Ohnishi-Kameyama, M., Sugie, H., Zungsontiporn, S., Fujii, Y., 1999. Three plant growth inhibiting saponins from *Duranta repens*. *Phytochemistry* 52, 1223–1228.
- Huan, V.D., Yamamura, S., Ohtani, K., Kasai, R., Yamasaki, K., Nham, N.T., Chau, H.M., 1998. Oleanane saponins from *Polyscias fruticosa*. *Phytochemistry* 47, 451–457.
- Huang, J., Ogihara, Y., Zhang, H., Shimizu, N., Takeda, T., 2000a. Ardisiamilliosides C–F, four new triterpenoid saponins from *Ardisia mamillata*. *Chemical and Pharmaceutical Bulletin* 48, 1413–1417.
- Huang, J., Ogihara, Y., Zhang, H., Shimizu, N., Takeda, T., 2000b. Triterpenoid saponins from *Ardisia mamillata*. *Phytochemistry* 54, 817–822.

- Huang, J., Wang, X., Ogihara, Y., Shimizu, N., Akiyama, T., Takeda, T., 2001a. Latifoliosides K and L, two new triterpenoid saponins from the bark of *Ilex latifolia*. Chemical and Pharmaceutical Bulletin 49, 765–767.
- Huang, J., Wang, X., Ogihara, Y., Shimizu, N., Takeda, T., Akiyama, T., 2001b. Latifoliosides I and J, two new triterpenoid saponins from the bark of *Ilex latifolia*. Chemical and Pharmaceutical Bulletin 49, 239–241.
- Huang, H.-C., Liao, S.-C., Chang, F.-R., Kuo, Y.-H., Wu, Y.-C., 2003. Molluscicidal saponins from *Sapindus mukorossi*, inhibitory agents of golden apple snails, *Pomacea canaliculata*. Journal of Agricultural and Food Chemistry 51, 4916–4919.
- Huong, N.T.T., Matsumoto, K., Kasai, R., Yamasaki, K., Watanabe, H., 1998a. In vitro antioxidant activity of Vietnamese ginseng saponin and its components. Biological and Pharmaceutical Bulletin 21, 978–981.
- Huong, N.T.T., Matsumoto, K., Watanabe, H., 1998b. The antistress effect of majonoside-R2, a major saponin component of Vietnamese ginseng: neuronal mechanism of action. Methods and Findings in Experimental and Clinical Pharmacology 20, 65–76.
- Iida, T., Yoshiki, Y., Okubo, K., Ohnui, H., Kinjo, J., Nohara, T., 1999. Triterpenoid saponins from *Vigna angularis*. Phytochemistry 51, 1055–1058.
- Iorizzi, M., Lanzotti, V., Ranalli, G., De Marino, S., Zollo, F., 2002. Antimicrobial furostanol saponins from the seeds of *Capsicum annuum* L. var. *acuminatum*. Journal of Agricultural and Food Chemistry 50, 4310–4316.
- Itabashi, M., Segawa, K., Ikeda, Y., Kondo, S., Naganawa, H., Koyano, T., Umezawa, K., 1999. A new bioactive steroidal saponin, furcraestatin, from the plant *Furcraea foetida*. Carbohydrate Research 323, 57–62.
- Jayasinghe, L., Hara, N., Fujimoto, Y., 2003. Bidesmosidic saponins from the fruits of *Diploclisia glaucescens*. Phytochemistry 62, 563–567.
- Jayatilake, G.S., Freeberg, D.R., Liu, Z., Richheimer, S.L., Blake, M.E., Bailey, D.T., Haridas, V., Gutterman, J.U., 2003. Isolation and structures of avicins D and G: in vitro tumor-inhibitory saponins derived from *Acacia victoriae*. Journal of Natural Products 66, 779–783.
- Jhoo, J.-W., Sang, S., He, K., Cheng, X., Zhu, N., Stark, R.E., Zheng, Q.Y., Rosen, R.T., Ho, C.-T., 2001. Characterization of the triterpene saponins of the roots and rhizomes of blue cohosh (*Caulophyllum thalictroides*). Journal of Agricultural and Food Chemistry 49, 5969–5974.
- Jia, Z., Koike, K., Kudo, M., Li, H., Nikaido, T., 1998a. Triterpenoid saponins and sapogenins from *Vaccaria segetalis*. Phytochemistry 48, 529–536.
- Jia, Z., Koike, K., Nikaido, T., 1998b. Major triterpenoid saponins from *Saponaria officinalis*. Journal of Natural Products 61, 1368–1373.
- Jia, Z., Koike, K., Nikaido, T., 1999. Saponarioside C, the first α -D-galactose containing triterpenoid saponin, and five related compounds from *Saponaria officinalis*. Journal of Natural Products 62, 449–453.
- Jiang, Z., Gallard, J.-F., Adeline, M.T., Dumontet, V., Tri, M.V., Sévenet, T., Pais, M., 1999. Six triterpenoid saponins from *Maesa laxiflora*. Journal of Natural Products 62, 873–876.
- Jin, S.-H., Park, J.-K., Nam, K.-Y., Park, S.-N., Jung, N.-P., 1999. Korean red ginseng saponins with low ratios of protopanaxadiol and protopanaxatriol saponin improve scopolamine-induced learning disability and spatial working memory in mice. Journal of Ethnopharmacology 66, 123–129.
- Johansson, M., Lövgren-Bengtsson, K., 1999. Isomers with different quillaja saponin components differ in their immunomodulating activities. Vaccine 17, 2894–2900.
- Junkuszew, M., Oleszek, W., Jurzysta, M., Piacente, S., Pizzi, C., 1998. Triterpenoid saponins from the seeds of *Amaranthus cruentus*. Phytochemistry 49, 195–198.
- Just, M.J., Recio, M.C., Giner, R.M., Cuéllar, M.J., Mñáez, S., Bilia, A.R., Ríos, J.-L., 1998. Anti-inflammatory activity of unusual lupane saponins from *Bupleurum frutescens*. Planta Medica 64, 404–407.
- Kamel, M.S., 1998. A furostanol saponin from fruits of *Balanites aegyptiaca*. Phytochemistry 48, 755–757.
- Kanchanapoom, T., Kasai, R., Yamasaki, K., 2001. Acetylated triterpene saponins from the Thai medicinal plant *Sapindus emarginatus*. Chemical and Pharmaceutical Bulletin 49, 1195–1197.
- Kang, S.S., Ahn, B.T., Kim, J.S., Bae, K., 1998. Lathyrus saponin, a new trisaccharide glycoside from *Lathyrus japonicus*. Journal of Natural Products 61, 299–300.
- Kanzaki, T., Morisaki, N., Shiina, R., Saito, Y., 1998. Role of transforming growth factor- β pathway in the mechanism of wound healing by saponin from Ginseng Radix rubra. British Journal of Pharmacology 125, 255–262.
- Kawata, Y., Kizu, H., Miyaichi, Y., Tomimori, T., 2001. Studies on the constituents of *Clematis* species. VIII. Triterpenoid saponins from the aerial part of *Clematis tibetana* Kuntz. Chemical and Pharmaceutical Bulletin 49, 635–638.
- Kersten, G.F.A., Crommelin, D.J.A., 2003. Liposomes and isomers. Vaccine 21, 915–920.
- Khalik, S.M.A., Miyase, T., El-Ashaal, H.A., Melek, F.R., 2000. Triterpenoid saponins from *Fagonia cretica*. Phytochemistry 54, 853–859.
- Killeen, G.F., Madigan, C.A., Connolly, C.R., Walsh, G.A., Clark, C., Hynes, M.J., Timmins, B.F., James, P., Headon, D.R., Power, R.F., 1998. Antimicrobial saponins of *Yucca schidigera* and the implications of their in vitro properties for their in vivo impact. Journal of Agricultural and Food Chemistry 46, 3178–3186.
- Kim, D.S., Oh, S.R., Lee, I.S., Jung, K.Y., Park, J.D., Kim, S.I., Lee, H.-K., 1998a. Anticomplementary activity of Ginseng saponins and their degradation products. Phytochemistry 47, 397–399.
- Kim, H.-S., Jang, C.-G., Oh, K.-W., Oh, S., Rheu, H.-M., Rhee, G.-S., Seong, Y.-H., Park, W.-K., 1998b. Effects of ginseng total saponin on morphine-induced hyperactivity and conditioned place preference in mice. Journal of Ethnopharmacology 60, 33–42.
- Kim, H.S., Kim, K.-S., 1999. Inhibitory effects of ginseng total saponin on nicotine-induced hyperactivity, reverse tolerance and dopamine receptor supersensitivity. Behavioural Brain Research 103, 55–61.
- Kim, H.-S., Kim, K.-S., Oh, K.-W., 1999. Ginseng total saponin inhibits nicotine-induced hyperactivity and conditioned place preference in mice. Journal of Ethnopharmacology 66, 83–90.
- Kinjo, J., Yokomizo, K., Hirakawa, T., Shii, Y., Nohara, T., Uyeda, M., 2000. Anti-herpes virus activity of fabaceous triterpenoidal saponins. Biological and Pharmaceutical Bulletin 23, 887–889.
- Kinoshita, K., Koyama, K., Takahashi, K., Kondo, N., Yuasa, H., 2000. A new triterpenoid saponin from *Isolatocereus dumortieri*. Journal of Natural Products 63, 701–703.
- Koike, K., Jia, Z., Nikaido, T., 1998. Triterpenoids saponins from *Vaccaria segetalis*. Phytochemistry 47, 1343–1349.
- Koike, K., Jia, Z., Nikaido, T., 1999a. New triterpenoid saponins and sapogenins from *Saponaria officinalis*. Journal of Natural Products 62, 1655–1659.
- Koike, K., Jia, Z., Ohura, S., Mochida, S., Nikaido, T., 1999b. Minor triterpenoid saponins from *Ardisia crenata*. Chemical and Pharmaceutical Bulletin 47, 434–435.
- Koike, K., Kudo, M., Jia, Z., Nikaido, T., Ide, Y., Sakura, T., 1999c. New triterpenoid saponins from *Maesa japonica*. Journal of Natural Products 62, 228–232.
- Koike, K., Jia, Z., Nikaido, T., 2001. New triterpenoids saponins from *Maesa tenera*. Chemical and Pharmaceutical Bulletin 49, 758–761.
- Kojima, K., Zhu, X.-B., Ogihara, Y., 1998. Saponins from *Gliricidia sepium*. Phytochemistry 48, 885–888.
- Konishi, M., Hano, Y., Takayama, M., Nomura, T., Hamzah, A.S., Ahmad, R.B., Jamani, H., 1998. Triterpenoid saponins from *Hedyotis nudicaulis*. Phytochemistry 48, 525–528.
- Konishi, T., Fujiwara, Y., Konoshima, T., Kiwosawa, S., Nishi, M., Miyahara, K., 2001. Steroidal saponins from *Hemerocallis fulva* var. *kwanso*. Chemical and Pharmaceutical Bulletin 49, 318–320.
- Kostova, I., Dinchev, D., Rentsch, G.H., Dimitrov, V., Ivanova, A., 2002. Two new sulfated furostanol saponins from *Tribulus terrestris*. Zeitschrift für Naturforschung C 57, 33–38.

- Kumara, S.S.M., Huat, B.T.K., 2001. Extraction, isolation and characterisation of antitumor principle, ϕ -hederin, from the seeds of *Nigella arvensis*. *Planta Medica* 67, 29–32.
- Kunert, O., Haslinger, E., Schmid, M.G., Reiner, J., Bucar, F., Mulatu, E., Abebe, D., Debelli, A., 2000. Three saponins, a steroid, and a flavanol glycoside from *Achyranthes aspera*. *Monatshefte für Chemie* 131, 195–204.
- Kuroda, M., Mimaki, Y., Hasegawa, F., Yokosuka, A., Sashida, Y., Sakagami, H., 2001. Steroidal glycosides from the bulbs of *Camassia leichlinii* and their cytotoxic activities. *Chemical and Pharmaceutical Bulletin* 49, 726–731.
- Kwak, W.J., Han, C.K., Chang, H.W., Kim, H.P., Kang, S.S., Son, K.H., 2003. Loniceroside C, an antiinflammatory saponin from *Lonicera japonica*. *Chemical and Pharmaceutical Bulletin* 51, 333–335.
- Lacaille-Dubois, M.A., Wagner, H., 1996. A review of the biological and pharmacological activities of saponins. *Phytomedicine* 2, 363–386.
- Lacaille-Dubois, M.-A., Hanquet, B., Cui, Z.-H., Lou, Z.-C., Wagner, H., 1999a. A new biologically active acylated triterpene saponin from *Silene fortunei*. *Journal of Natural Products* 62, 133–136.
- Lacaille-Dubois, M.-A., Hanquet, B., Cui, Z.-H., Lou, Z.-C., Wagner, H., 1999b. A new biologically active acylated triterpene saponin from *Silene fortunei*. *Journal of Natural Products* 62, 404.
- Larhsini, M., Marston, A., Hostettmann, K., 2003. Triterpenoid saponins from the roots of *Silene cucubalus*. *Fitoterapia* 74, 237–241.
- Lavaud, C., Voutquenne, L., Massiot, G., Le Men-Olivier, L., Das, B.C., Laprévote, O., Serani, L., Delaude, C., Becchi, M., 1998. Saponins from the stem bark of *Filicium decipiens*. *Phytochemistry* 47, 441–449.
- Lavaud, C., Voutquenne, L., Bal, P., Pouny, I., 2000. Saponins from *Chenopodium album*. *Fitoterapia* 71, 338–340.
- Lavaud, C., Crublet, M.-L., Pouny, I., Litaudon, M., Sévenet, T., 2001. Triterpenoid saponins from the stem bark of *Elattostachys apetala*. *Phytochemistry* 57, 469–478.
- Lee, B.-H., Lee, S.-J., Hui, J.-H., Lee, S., Sung, J.-H., Huh, J.D., Moon, C.-K., 1998. In vitro antigenotoxic activity of novel ginseng saponin metabolites formed by intestinal bacteria. *Planta Medica* 64, 500–503.
- Lee, S.-J., Sung, J.-H., Lee, S.-J., Moon, C.-K., Lee, B.-H., 1999. Antitumor activity of a novel ginseng saponin metabolite in human pulmonary adenocarcinoma cells resistant to cisplatin. *Cancer Letters* 144, 39–43.
- Lee, S.-C., Moon, Y.-S., You, K.-H., 2000. Effects of red ginseng saponins and nootropic drugs on impaired acquisition of ethanol-treated rats in passive avoidance performance. *Journal of Ethnopharmacology* 69, 1–8.
- Li, T., Yuying, Z., Guangzhong, T., Bin, W., Shaoqing, C., Ruyi, Z., 1999a. Saikosaponins from roots of *Bupleurum scorzonrifolium*. *Phytochemistry* 50, 139–142.
- Li, X.-C., ElSohly, H.N., Nimrod, A.C., Clark, A.M., 1999b. Antifungal jujubogenin saponins from *Colubrina retusa*. *Journal of Natural Products* 62, 674–677.
- Li, D.W., Lee, E.B., Kang, S.S., Hyun, J.E., Whang, W.K., 2002. Activity-guided isolation of saponins from *Kalopanax pictus* with anti-inflammatory activity. *Chemical and Pharmaceutical Bulletin* 50, 900–903.
- Liao, B., Newmark, H., Zhou, R., 2002. Neuroprotective effects of ginseng total saponin and ginsenosides Rb₁ and Rg₁ on spinal cord neurons in vitro. *Experimental Neurology* 173, 224–234.
- Liu, W.K., Xu, S.X., Che, C.T., 2000. Anti-proliferative effect of ginseng saponins on human prostate cancer cell line. *Life Sciences* 67, 1297–1306.
- Liu, J., Henkel, T., 2002. Traditional Chinese medicine (TCM): are polyphenols and saponins the key ingredients triggering biological activities? *Current Medicinal Chemistry* 9, 1483–1485.
- Lu, Y., Umeda, T., Yagi, A., Sakata, K., Chaudhuri, T., Ganguly, D.K., Sarma, S., 2000. Triterpenoid saponins from the roots of tea plant (*Camellia sinensis* var. *assamica*). *Phytochemistry* 53, 941–946.
- Ma, W.G., Mizutani, M., Malterud, K.E., Lu, S.L., Ducrey, B., Tahara, S., 1999. Saponins from the roots of *Panax notoginseng*. *Phytochemistry* 52, 1133–1139.
- Ma, J., He, F.-H., Deng, J.-Z., Ye, W.-C., Zhao, S.-X., Wu, H.-M., 2001. Triterpenoid saponins from *Vaccaria segetalis*. *Chinese Journal of Chemistry* 19, 606–611.
- Marciani, D.J., Athak, A.K., Reynolds, R.C., Seitz, L., May, R.D., 2001. Altered immunomodulating and toxicological properties of degraded *Quillaja saponaria* Molina saponins. *International Immunopharmacology* 1, 813–818.
- Marquina, S., Maldonado, N., Garduño-Ramírez, M.L., Aranda, E., Villarreal, M.L., Navarro, V., Bye, R., Delgado, G., Alvarez, L., 2001. Bioactive oleanolic acid saponins and other constituents from the roots of *Viguiera decurrens*. *Phytochemistry* 56, 93–97.
- Matsuda, H., Murakami, T., Ikebata, A., Yamahara, J., Yoshikawa, M., 1999. Bioactive saponins and glycosides. XIV. Structure elucidation and immunological adjuvant activity of novel protojubenin type triterpene bisdesmosides, protojubenosides A, B, and B₁, from the seeds of *Zizyphus jujuba* var. *spinosa* (Zizyphi Spinosi Semen). *Chemical and Pharmaceutical Bulletin* 47, 1744–1748.
- Matsuda, H., Morikawa, T., Ueda, H., Yoshikawa, M., 2001. Medicinal foodstuffs. XXVII. Saponin constituents of gotu kola (2): structures of new ursane- and oleanane-type triterpene oligoglycosides, centellasaponins B, C, and D, from *Centella asiatica* cultivated in Sri Lanka. *Chemical and Pharmaceutical Bulletin* 49, 1368–1371.
- Matsuura, H., 2001. Saponins in garlic as modifiers of the risk of cardiovascular disease. *The Journal of Nutrition* 131, 1000S–1005S.
- Melek, F.R., Miyase, T., Ghaly, N.S., 2003. Triterpenoid saponins from *Meryta lanceolata*. *Phytochemistry* 62, 557–562.
- Meslehy, M.R., 1998. Hopane-type saponins from *Polycarpon succulentum*—II. *Phytochemistry* 48, 1415–1421.
- Michl, G., Abebe, D., Bucar, F., Debelli, A., Kunert, O., Schmid, M.G., Mulatu, E., Haslinger, E., 2000. New triterpenoid saponins from *Achyranthes aspera* Linn. *Helvetica Chimica Acta* 83, 359–363.
- Mimaki, Y., Kuroda, M., Kameyama, A., Yokosuka, A., Sashida, Y., 1998a. Aculeoside B, a new bisdesmosidic spirostanol saponin from the underground parts of *Ruscus aculeatus*. *Journal of Natural Products* 61, 1279–1282.
- Mimaki, Y., Kuroda, M., Kameyama, A., Yokosuka, A., Sashida, Y., 1998b. Steroidal saponins from the underground parts of *Ruscus aculeatus* and their cytostatic activity on HL-60 cells. *Phytochemistry* 48, 485–493.
- Mimaki, Y., Kuroda, M., Kameyama, A., Yokosuka, A., Sashida, Y., 1998c. Steroidal saponins from the rhizomes of *Hosta sieboldii* and their cytostatic activity on HL-60 cells. *Phytochemistry* 48, 1361–1369.
- Mimaki, Y., Kuroda, M., Takaashi, Y., Sashida, Y., 1998d. Steroidal saponins from the leaves of *Cordyline stricta*. *Phytochemistry* 47, 79–85.
- Mimaki, Y., Kuroda, M., Takaashi, Y., Sashida, Y., 1998e. Steroidal saponins from the stems of *Dracaena concinna*. *Phytochemistry* 47, 1351–1356.
- Mimaki, Y., Kuroda, M., Asano, T., Sashi, Y., 1999a. Triterpene saponins and lignans from the roots of *Pulsatilla chinensis* and their cytotoxic activity against HL-60 cells. *Journal of Natural Products* 62, 1279–1283.
- Mimaki, Y., Kuroda, M., Fukasawa, T., Sashida, Y., 1999b. Steroidal saponins from the bulbs of *Allium karataviense*. *Chemical and Pharmaceutical Bulletin* 47, 738–743.
- Mimaki, Y., Kuroda, M., Ide, A., Kameyama, A., Yokosuka, A., Sashida, Y., 1999c. Steroidal saponins from the aerial parts of *Dracaena draco* and their cytostatic activity on HL-60 cells. *Phytochemistry* 50, 805–813.
- Mimaki, Y., Kuora, M., Yokosuka, A., Sashida, Y., 1999d. A spirostanol saponin from the underground parts of *Ruscus aculeatus*. *Phytochemistry* 51, 689–692.
- Mimaki, Y., Satou, T., Kuroda, M., Sashida, Y., Hatakeyama, Y., 1999e. Steroidal saponins from the bulbs of *Lilium candidum*. *Phytochemistry* 51, 567–573.
- Mimaki, Y., Watanabe, K., Ando, Y., Sakuma, C., Sashida, Y., Furuya, S., Sakagami, H., 2001a. Flavonol glycosides and steroidal saponins

- from the leaves of *Cestrum nocturnum* and their cytotoxicity. Journal of Natural Products 64, 17–22.
- Mimaki, Y., Yokosuka, A., Kuroda, M., Sashida, Y., 2001b. Cytotoxic activities and structure–cytotoxic relationships of steroidal saponins. Biological and Pharmaceutical Bulletin 24, 1286–1289.
- Mitaine-Offier, A.-C., Marouf, A., Hanquet, B., Birlirakis, N., Lacaille-Dubois, M.-A., 2001a. Two triterpene saponins from *Achyranthes bidentata*. Chemical and Pharmaceutical Bulletin 49, 1492–1494.
- Mitaine-Offier, A.C., Marouf, A., Pizza, C., Khanh, T.C., Chauffert, B., Lacaille-Dubois, M.-A., 2001b. Bidentatoside I, a new triterpene saponin from *Achyranthes bidentata*. Journal of Natural Products 64, 243–245.
- Mitaine-Offier, A.-C., Miyamoto, T., Khan, I.A., Delaude, C., Lacaille-Dubois, M.-A., 2002. Three new triterpene saponins from two species of *Carpolobia*. Journal of Natural Products 65, 553–557.
- Miyakoshi, M., Shirasuna, K., Hirai, Y., Shingu, K., Isoda, S., Shoji, J., Ida, Y., Shimizu, T., 1999. Triterpenoid saponins from *Acanthopanax nipponicus* leaves. Journal of Natural Products 62, 445–448.
- Miyakoshi, M., Tamura, Y., Masuda, H., Mizutani, K., Tanaka, O., Ikeda, T., Ohtani, K., Kasai, R., Yamasaki, K., 2000. Antiyeast steroidal saponins from *Yucca schidigera* (*Mohave yucca*), a new anti-food-deteriorating agent. Journal of Natural Products 63, 332–338.
- Mølgaard, P., Chihaka, A., Lemmich, E., Furu, P., Windber, C., Ingerslev, F., Halling-Sørensen, B., 2000. Biodegradability of the molluscicidal saponins of *Phytolacca dodecandra*. Regulatory Toxicology and Pharmacology 32, 248–255.
- Mshvildadze, V., Favel, A., Delmas, F., Elias, R., Faure, R., Decanosidze, G., Kemertelidze, E., Balansard, G., 2000. Antifungal and antiprotozoal activities of saponins from *Hedera colchica*. Pharmazie 55, 325–326.
- Mshvildadze, V., Elias, R., Faure, R., Debrauwer, L., Dekanosidze, G., Kemertelidze, E., Balansard, G., 2001. Triterpenoid saponins from berries of *Hedera colchica*. Chemical and Pharmaceutical Bulletin 49, 752–754.
- Mujoo, K., Haridas, V., Hoffmann, J.J., Wächter, G.A., Hutter, L.K., Lu, Y., Blake, M.E., Jayatilake, G.S., Bailey, D., Mills, G.B., Guterman, J.U., 2001. Triterpenoid saponins from *Acacia victoriae* (Benth) decrease tumor cell proliferation and induce apoptosis. Cancer Research 61, 5486–5490.
- Murakami, T., Matsuda, H., Inadzuki, M., Hirano, K., Yoshikawa, M., 1999a. Medicinal foodstuffs. XVI. Sugar beet (3): absolute stereostructures of betavulgarosides II and IV, hypoglycemic saponins having a unique substituent, from the roots of *Beta vulgaris* L. Chemical and Pharmaceutical Bulletin 47, 1717–1724.
- Murakami, T., Nakamura, J., Matsuda, H., Yoshikawa, M., 1999b. Bioactive saponins and glycosides. XV. Saponin constituents with gastroprotective effect from the seeds of tea plant, *Camellia sinensis* L. var. *assamica* PIERRE, cultivated in Sri Lanka: structures of assamsaponins A, B, C, D, and E. Chemical and Pharmaceutical Bulletin 47, 1759–1764.
- Murakami, T., Kishi, A., Matsuda, H., Yoshikawa, M., 2000a. Medicinal foodstuffs. XVII. Fenugreek seed (3): structures of new furostanol-type steroid saponins, trigoneosides Xa, Xb, Xlb, Xlla, Xlib, and Xllla, from the seeds of Egyptian *Trigonella foenum-graecum* L. Chemical and Pharmaceutical Bulletin 48, 994–1000.
- Murakami, T., Nakamura, J., Kageura, T., Matsuda, H., Yoshikawa, M., 2000b. Bioactive saponins and glycosides. XVII. Inhibitory effect on gastric emptying and accelerating effect on gastrointestinal transit of tea saponins: structures of assamsaponins F, G, H, I and J from the seeds and leaves of the tea plant. Chemical and Pharmaceutical Bulletin 48, 1720–1725.
- Murakami, T., Emoto, A., Matsuda, H., Yoshikawa, M., 2001a. Medicinal foodstuffs. XXI. Structures of new cucurbitane-type triterpene glycosides, goglycosides-a, -b, -c, -d, -e, -f, -g, and -h, and new oleanane-type triterpene saponins, goyasaponins I, II, and III, from the fresh fruit of Japanese *Momordica charantia* L. Chemical and Pharmaceutical Bulletin 49, 54–63.
- Murakami, T., Oominami, H., Matsuda, H., Yoshikawa, M., 2001b. Bioactive saponins and glycosides. XVIII. Nortriterpene and triterpene oligoglycosides from the fresh leaves of *Euptelea polyandra* Sieb. et. Zucc (2): structures of eupteleasaponins VI, VI acetate, VII, VIII, IX, X, XI, and XII. Chemical and Pharmaceutical Bulletin 49, 741–746.
- Navarro, P., Giner, R.M., Recio, M.C., Máñez, S., Cerdá-Nicolás, M., Ríos, J.-L., 2001. In vivo anti-inflammatory activity of saponins from *Bupleurum rotundifolium*. Life Sciences 68, 1199–1206.
- Ngounou, F.N., Atta-ur-Rahman, Choudhary, M.I., Malik, S., Zareen, S., Ali, R., Lontsi, D., Sondengam, B.L., 1999. Two saponins from *Pteleopsis hylodendron*. Phytochemistry 52, 917–921.
- Nikaido, T., Koike, K., Mitsunaga, K., Saeki, T., 1999. Two new triterpenoid saponins from *Platycodon grandiflorum*. Chemical and Pharmaceutical Bulletin 47, 903–904.
- Nishimura, K., Miyase, T., Noguchi, H., 1999. Triterpenoid saponins from *Ilex kudinchia*. Journal of Natural Products 62, 1128–1133.
- Nocerino, E., Amato, M., Izzo, A.A., 2000. The aphrodisiac and adaptogenic properties of ginseng. Fitoterapia 71, S1–S5.
- Oda, K., Matsuda, H., Murakami, T., Katayama, S., Ohgitani, T., Yoshikawa, M., 2000. Adjuvant and haemolytic activities of 47 saponins derived from medicinal and food plants. Biological Chemistry 381, 67–74.
- Oda, K., Matsuda, H., Murakami, T., Katayama, S., Ohgitani, T., Yoshikawa, M., 2003. Relationship between adjuvant activity and amphipathic structure of soyasaponins. Vaccine 21, 2145–2151.
- Oleszek, W., Junkuszew, M., Stochmal, A., 1999. Determination and toxicity of saponins from *Amaranthus cruentus*. Journal of Agricultural and Food Chemistry 47, 3685–3687.
- Oleszek, W., Sitek, M., Stochmal, A., Piacente, S., Pizza, C., Cheeke, P., 2001. Steroidal saponins of *Yucca schidigera* Roetz. Journal of Agricultural and Food Chemistry 49, 4392–4396.
- Oleszek, W., Stochmal, A., 2002. Triterpene saponins and flavonoids in the seeds of *Trifolium* species. Phytochemistry 61, 165–170.
- Olugbade, T.A., Ogundaini, A., Birlirakis, N., País, M., Martin, M.-T., 2000. Petersaponins III and IV, triterpenoid saponins from *Petersianthus macrocarpus*. Journal of Natural Products 63, 716–719.
- Osborn, A.E., 2003. Molecules of interest, saponins in cereals. Phytochemistry 62, 1–4.
- Ouyang, M.-A., Liu, Y.-Q., Wang, H.-Q., Yang, C.-R., 1998. Triterpenoid saponins from *Ilex latifolia*. Phytochemistry 49, 2483–2486.
- Parab, R.S., Mengi, S.A., 2002. Hypolipidemic activity of *Acorus calamus* L. in rats. Fitoterapia 73, 451–455.
- Park, H.-J., Kwon, S.-H., Lee, J.-H., Lee, K.-H., Miyamoto, K.I., Lee, K.-T., 2001. Kalopanaxsaponin A is a basic saponin structure for the anti-tumor activity of hederagenin monodesmosides. Planta Medica 67, 118–121.
- Pawar, R., Gopalakrishnan, C., Bhutani, K.K., 2001. Dammarane triterpene saponin from *Bacopa monniera* as the superoxide inhibitor in polymorphonuclear cells. Planta Medica 67, 752–754.
- Plock, A., Beyer, G., Hiller, K., Gründemann, E., Krause, E., Nimtz, M., Wray, V., 2001. Application of MS and NMR to the structure elucidation of complex sugar moieties of natural products: exemplified by the steroidal saponins from *Yucca filamentosa* L. Phytochemistry 57, 489–496.
- Pöhlmann, K., Schaller, K., Schweizer, U., Elgama, M.H.A., Shaker, K.H., Seifert, K., 1998. Triterpenoid saponins from *Zygophyllum decumbens*. Phytochemistry 48, 875–880.
- Putalun, W., Xuan, L.-J., Tanaka, H., Shoyama, Y., 1999. Solakhasoside, a novel steroidal saponin from *Solanum khasianum*. Journal of Natural Products 62, 181–183.
- Qiu, S.-X., Li, X.-C., Xiong, Y., Dong, Y., Chai, H., Farnsworth, N.R., Pezzuto, J.M., Fong, H.H.S., 2000. Isolation and characterization of cytotoxic saponin chloromaloside A from *Chlorophytum malayense*. Planta Medica 66, 587–590.
- Quiroga, E.N., Sampietro, A.R., Vattuone, M.A., 2001. Screening antifungal activities of selected medicinal plants. Journal of Ethnopharmacology 74, 89–96.
- Rastrelli, L., Aquino, R., Abdo, S., Proto, M., De Simone, F., De Tommasi, N., 1998. Studies on the constituents of *Amaranthus caudatus* leaves:

- isolation and structure elucidation of new triterpenoid saponins and ionol-derived glycosides. *Journal of Agricultural and Food Chemistry* 46, 1797–1804.
- Rastrelli, L., Caceres, A., De Simone, F., Aquino, R., 1999. Studies on the constituents of *Gliricidia sepium* (Leguminosae) leaves and roots: isolation and structure elucidation of new triterpenoid saponins and aromatic compounds. *Journal of Agricultural and Food Chemistry* 47, 1537–1540.
- Safir, O., Fkih-Tetouani, S., de Tommasi, N., Aquino, R., 1998. Saponins from *Zygophyllum gaetulum*. *Journal of Natural Products* 61, 130–134.
- Sahpaz, S., Gupta, M.P., Hostettmann, K., 2000. Triterpene saponins from *Randia formosa*. *Phytochemistry* 54, 77–84.
- Sahu, N.P., Koike, K., Banerjee, S., Achari, B., Nikaido, T., 2001. Triterpenoid saponins from *Mollugo spargula*. *Phytochemistry* 58, 1177–1182.
- Sakai, K., Nagao, T., Okabe, H., 1999. Triterpenoid saponins from the ground part of *Aster ageratoides* var. *ovatus*. *Phytochemistry* 51, 309–318.
- Sánchez-Contreras, S., Díaz-Lanza, A.M., Matellano, L.F., Bernabé, M., Ollivier, E., Balansard, G., Faure, R., 1998. A sulfated saponin from *Bupleurum rigidum*. *Journal of Natural Products* 61, 1383–1385.
- Sánchez-Contreras, S., Díaz-Lanza, A.M., Bernabé, M., 2000. Four new triterpenoid saponins from the roots of *Bupleurum rigidum*. *Journal of Natural Products* 63, 1479–1482.
- Sang, S., Lao, A., Wang, H., Chen, Z., 1999a. Two new spirostanol saponins from *Allium tuberosum*. *Journal of Natural Products* 62, 1028–1029.
- Sang, S., Lao, A., Wang, H., Chen, Z., 1999b. Furostanol saponins from *Allium tuberosum*. *Phytochemistry* 52, 1611–1615.
- Sang, S., Mao, S., Lao, A., Chen, Z., Ho, C.-T., 2001a. Four new steroidal saponins from the seeds of *Allium tuberosum*. *Journal of Agricultural and Food Chemistry* 49, 1475–1478.
- Sang, S., Zou, M., Xia, Z., Lao, A., Chen, Z., Ho, C.-T., 2001b. New spirostanol saponins from Chinese chives (*Allium tuberosum*). *Journal of Agricultural and Food Chemistry* 49, 4780–4783.
- Sanoko, R., Speranza, G., Pizza, C., De Tommasi, N., 1999. Triterpene saponins from *Alternanthera repens*. *Phytochemistry* 51, 1043–1047.
- Scarpato, R., Bertoli, A., Naccarati, A., Migliore, L., Cocchi, L., Barale, R., Pistelli, L., 1998. Different effects of newly isolated saponins on the mutagenicity and cytotoxicity of the anticancer drugs mitomycin C and bleomycin in human lymphocytes. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis* 420, 49–54.
- Schühly, W., Heilmann, J., Čalis, I., Sticher, O., 2000. Novel triterpene saponins from *Zizyphus joazeiro*. *Helvetica Chimica Acta* 83, 1509–1516.
- Seo, Y., Berger, J.M., Hoch, J., Neddermann, K.M., Burscher, I., Mamber, S.W., Kingston, D.G.I., 2002a. A new triterpene saponin from *Pittosporum viridiflorum* from the Madagascar rainforest. *Journal of Natural Products* 65, 65–68.
- Seo, Y., Hoch, J., Abdel-Kader, M., Malone, S., Derveld, I., Adams, H., Werkhoven, M.C.M., Wisse, J.H., Mamber, S.W., Dalton, J.M., Kingston, D.G.I., 2002b. Bioactive saponins from *Acacia tenuifolia* from the Suriname rainforest. *Journal of Natural Products* 65, 170–174.
- Shaker, K.H., Bernhardt, M., Elgamal, M.H.A., Seifert, K., 1999. Triterpenoid saponins from *Fagonia indica*. *Phytochemistry* 51, 1049–1053.
- Shaker, K.H., Bernhardt, M., Hani, M., Elgamal, A., Seifert, K., 2001. Triterpenoid saponins from *Astragalus trigonus*. *Zeitschrift für Naturforschung C* 56, 699–702.
- Shen, P., Wang, S.-L., Liu, X.-K., Yang, C.-R., Cai, B., Yao, X.-S., 2003. Steroidal saponins from rhizomes of *Tupistra wattii* Hook. f. *Chemical and Pharmaceutical Bulletin* 51, 305–308.
- Shibata, S., 2001. Chemistry and cancer preventing activities of ginseng saponins and some related triterpenoid compounds. *Journal of Korean Medical Science* 16, S28–37.
- Shin, M.H., Wang, W., Nam, K.I., Jo, Y., Jung, J.H., Im, K.S., 2003. Triterpenoid saponins from the fruits of *Ternstroemia japonica*. *Journal of Natural Products* 66, 1351–1355.
- Simões, C.M.O., Amoroso, M., Girre, L., 1999. Mechanism of antiviral activity of triterpenoid saponins. *Phytotherapy Research* 13, 323–328.
- Simonet, A.M., Stochmal, A., Oleszek, W., Macias, F.A., 1999. Saponins and polar compounds from *Trifolium resupinatum*. *Phytochemistry* 51, 1065–1067.
- Sindambiwe, J.B., Calomme, M., Geerts, S., Pieters, L., Vlietinck, A.J., Vanden Berghe, D.A., 1998. Evaluation of biological activities of triterpenoid saponins from *Maesa lanceolata*. *Journal of Natural Products* 61, 585–590.
- Sirtori, C.R., 2001. Aescin: Pharmacology, pharmacokinetics and therapeutic profile. *Pharmacological Research* 44, 183–193.
- Sjölander, A., Cox, J.C., 1998. Uptake and adjuvant activity of orally delivered saponin and ISCOM™ vaccines. *Advanced Drug Delivery Reviews* 34, 321–338.
- Soliman, H.S.M., Elgamal, M.H.A., Simon, A., Tóth, G., Horváth, G., Duddeck, H., 1999. A new gypsogenin saponin from *Arenaria filicaulis*. *Journal of Natural Products* 62, 885–888.
- Soliman, H.S.M., Simon, A., Tóth, G., Duddeck, H., 2001. Identification and structure determination of four triterpene saponins from some Middle-East plants. *Magnetic Resonance in Chemistry* 39, 567.
- Song, S.-J., Nakamura, N., Ma, C.-M., Hattori, M., Xu, S.-X., 2000. Four new saponins from the root bark of *Aralia elata*. *Chemical and Pharmaceutical Bulletin* 48, 838–842.
- Song, S.-J., Nakamura, N., Ma, C.-M., Hattori, M., Xu, S.-X., 2001. Five saponins from the root bark of *Aralia elata*. *Phytochemistry* 56, 491–497.
- Su, Y., Guo, D., Guo, H., Liu, J., Zheng, J., Koike, K., Nikaido, T., 2001. Four new triterpenoid saponins from *Conyza blinii*. *Journal of Natural Products* 64, 32–36.
- Su, Y., Koike, K., Nikaido, T., Liu, J., Zheng, J., Guo, D., 2003. Conyzasaponins I–Q, nine new triterpenoid saponins from *Conyza blinii*. *Journal of Natural Products* 66, 1593–1599.
- Tanaka, O., Han, E.-C., Yamaguchi, H., Matsuura, H., Murakami, T., Taniyama, T., Yoshikawa, M., 2000. Saponins of plants of *Panax* species collected in central Nepal, and their chemotaxonomical significance. III. *Chemical and Pharmaceutical Bulletin* 48, 889–892.
- Tapondjou, L.A., Lontsi, D., Sondengam, B.L., Shaheen, F., Choudhary, M.I., Atta-ur-Rahman, , Van Heerden, F.R., Park, H.-J., Lee, K.-T., 2003. Saponins from *Cussonia bancoensis* and their inhibitory effects on nitric oxide production. *Journal of Natural Products* 66, 1266–1269.
- Tezuka, Y., Honda, K., Banskota, A.J., Thet, M.M., Kadota, S., 2000. Kinmoonosides A–C, three new cytotoxic saponins from the fruits of *Acacia concinna*, a medicinal plant collected in Myanmar. *Journal of Natural Products* 63, 1658–1664.
- Tran, Q.L., Adnyana, I.K., Tezuka, Y., Nagaoka, T., Tran, Q.K., Kadota, S., 2001a. Triterpene saponins from Vietnamese ginseng (*Panax vietnamensis*) and their hepatocytoprotective activity. *Journal of Natural Products* 64, 456–461.
- Tran, Q.L., Tezuka, Y., Banskota, A.H., Tran, Q.K., Saiki, I., Kadota, S., 2001b. New spirostanol steroids and steroidal saponins from roots and rhizomes of *Dracaena angustifolia* and their antiproliferative activity. *Journal of Natural Products* 64, 1127–1132.
- Tran, Q.L., Adnyana, I.K., Tezuka, Y., Harimaya, Y., Saiki, I., Kurashige, Y., Tran, Q.K., Kadota, S., 2002. Hepatoprotective effect of majonoside R₂, the major saponin from Vietnamese ginseng (*Panax vietnamensis*). *Planta Medica* 68, 402–406.
- Traore, F., Faure, R., Olivier, E., Gasquet, M., Azas, N., Debrauwer, L., Keita, A., Timon-David, P., Balansard, G., 2000. Structure and antiprotozoal activity of triterpenoid saponins from *Glinus oppositifolius*. *Planta Medica* 66, 368–371.
- Treyvaud, V., Marston, A., Dyatmiko, W., Hostettmann, K., 2000. Moluscicidal saponins from *Phytolacca icosandra*. *Phytochemistry* 55, 603–609.
- Tyler, V.E., Brady, L.R., Robbers, J.E., 1981. *Pharmacognosy*, eighth ed. Lea & Febiger, Philadelphia, p. 67 (ISBN 0-8121-0793-4).
- Udayama, M., Kinjo, J., Nohara, T., 1998. Triterpenoid saponins from *Baptisia australis*. *Phytochemistry* 48, 1233–1235.

- Ueckert, J., Wray, V., Nimtz, M., Schöpke, T., 1998. Noroleanane saponins from *Celmisia spectabilis*. *Phytochemistry* 49, 2487–2492.
- Um, B.-H., Weniger, B., Lobstein, A., Pouplin, T., Polat, M., Aragón, R., Anton, R., 2001. Triterpenoid saponins from *Iseria pittieri*. *Journal of Natural Products* 64, 1588–1589.
- Une, H.D., Sarveiya, V.P., Pal, S.C., Kasture, V.X., Kasture, S.B., 2001. Nootropic and anxiolytic activity of saponins of *Albizia lebbek* leaves. *Pharmacology Biochemistry and Behavior* 69, 439–444.
- Verotta, L., Guerrini, M., El-Sebakhy, N.A., Assad, A.M., Toaima, S.M., Radwan, M.M., Luo, Y.-D., Pezzuto, J.M., 2002. Cycloartane and oleanane saponins from Egyptian *Astragalus* spp. as modulators of lymphocyte proliferation. *Planta Medica* 68, 986–994.
- Voutquenne, L., Lavaud, C., Massiot, G., Delaude, C., 1998. Saponins from *Harpullia cupanioides*. *Phytochemistry* 49, 2081–2085.
- Voutquenne, L., Kokougan, C., Lavaud, C., Pouny, I., Litaudon, M., 2002. Triterpenoid saponins and acylated prosapogenins from *Harpullia austro-caledonica*. *Phytochemistry* 59, 825–832.
- Voutquenne, L., Guinot, P., Thoison, O., Sevenet, T., Lavaud, C., 2003. Oleanolic glycosides from *Pometia ridleyi*. *Phytochemistry* 64, 781–789.
- Wandji, J., Tillequin, F., Mulholland, D.A., Shirri, J.C., Tsabang, N., Seguin, E., Verite, P., Libot, F., Fomum, Z.T., 2003. Pentacyclic triterpenoid and saponins from *Gambeya boukokoensis*. *Phytochemistry* 64, 845–849.
- Wang, M.-K., Cai, H., Peng, S.-L., Ding, L.-S., Wu, F.-E., Chen, Y.-Z., 1998. Triterpenoid saponins from *Berneuxia thebetica*. *Phytochemistry* 48, 1411–1414.
- Wang, H.X., Ng, T.B., 1999. Natural products with hypoglycaemic, hypotensive, hypocholesterolemic, antiatherosclerotic and antithrombotic activities. *Life Sciences* 65, 2663–2677.
- Wang, B.-G., Zhu, W.-M., Li, X.-M., Jia, Z.-J., Hao, X.-J., 2000. Rubupungenosides A and B, two novel triterpenoid saponin dimers from the aerial parts of *Rubus pungens*. *Journal of Natural Products* 63, 851–854.
- Wang, Z., Zhou, J., Ju, Y., Zhang, H., Liu, M., Li, X., 2001. Effects of two saponins extracted from the *Polygonatum zanlanscianense* pamp on the human leukemia (HL-60) cells. *Biological and Pharmaceutical Bulletin* 24, 159–162.
- Watanabe, K., Mimaki, Y., Sakuma, C., Sashida, Y., 2003. Eranthisaponins A and B, two new bisdesmosidic triterpene saponins from the tubers of *Eranthis cilicica*. *Journal of Natural Products* 66, 879–882.
- Withavaskul, P., Panthong, A., Danjanapothi, D., Taesothikul, T., Lertprasertsuke, N., 2003. Acute and subacute toxicities of the saponin mixture isolated from *Schefflera leucantha* Viguier. *Journal of Ethnopharmacology* 89, 115–121.
- Woldemichael, G.M., Wink, M., 2001. Identification and biological activities of triterpenoid saponins from *Chenopodium quinoa*. *Journal of Agricultural and Food Chemistry* 49, 2327–2332.
- Woldemichael, G.M., Montenegro, G., Timmermann, B.N., 2003. Triterpenoidal lupin saponins from the Chilean legume *Lupinus oreophilus* Phil. *Phytochemistry* 63, 853–857.
- Xiang, T., Tezuka, Y., Wu, L.-J., Banskota, A.H., Kadota, S., 2000. Saponins from *Lonicera bournei*. *Phytochemistry* 54, 795–799.
- Xiao, K., Yi, Y.-H., Wang, Z.-Z., Tang, H.-F., Li, Y.-Q., Lin, H.-W., 1999. A cytotoxic triterpene saponin from the root bark of *Aralia dasyphylla*. *Journal of Natural Products* 62, 1030–1032.
- Xu, Y.-X., Chen, H.-S., Liang, H.-Q., Gu, Z.-B., Liu, W.-Y., Leung, W.-N., Li, T.-J., 2000. Three new saponins from *Tribulus terrestris*. *Planta Medica* 66, 545–550.
- Yang, X.-W., Zhao, J., Cui, Y.-X., Liu, X.-H., Ma, C.-M., Hattori, M., Zhang, L.-H., 1999. Anti-HIV-1 protease triterpenoid saponins from the seeds of *Aesculus chinensis*. *Journal of Natural Products* 62, 1510–1513.
- Yang, D.-J., Lu, T.-J., Hwang, L.S., 2003. Isolation and identification of steroidal saponins in Taiwanese yam cultivar (*Dioscorea pseudo-japonica* Yamamoto). *Journal of Agricultural and Food Chemistry* 51, 6438–6444.
- Yayla, Y., Alankuş-Çalışkan, Ö., Anıl, H., Bates, R.B., Stessman, C.C., Kane, V.V., 2002. Saponins from *Styrax officinalis*. *Fitoterapia* 73, 320–326.
- Yayli, N., Baltacı, C., Zengin, A., Kuçukislaoglu, M., Genc, H., 1998. A triterpenoid saponin from *Cyclamen coum*. *Phytochemistry* 48, 881–884.
- Ye, W., Pan, G., Zhang, Q., Che, C.-T., Wu, H., Zhao, S., 1999. Five new triterpene saponins from *Pulsatilla patens* var. *multifida*. *Journal of Natural Products* 62, 233–237.
- Ye, W.-C., Zhang, Q.-W., Liu, X., Che, C.-T., Zhao, S.-X., 2000. Oleanane saponins from *Gymnema sylvestre*. *Phytochemistry* 53, 893–899.
- Ye, W., Liu, X., Zhang, Q., Che, C.-T., Zhao, S., 2001. Antisweet saponins from *Gymnema sylvestre*. *Journal of Natural Products* 64, 232–235.
- Yeşilada, E., Takaishi, Y., 1999. A saponin with anti-ulcerogenic effect from the flowers of *Spartium junceum*. *Phytochemistry* 51, 903–908.
- Yokosuka, A., Mimaki, Y., Kuroda, M., Sashida, Y., 2000a. A new steroidal saponin from the leaves of *Agave americana*. *Planta Medica* 66, 393–396.
- Yokosuka, A., Mimaki, Y., Sashida, Y., 2000b. Steroidal saponins from *Dracaena surculosa*. *Journal of Natural Products* 63, 1239–1243.
- Yokosuka, A., Mimaki, Y., Sashida, Y., 2002a. Four new 3,5-cyclosteroidal saponins from *Dracaena surculosa*. *Chemical and Pharmaceutical Bulletin* 50, 992–995.
- Yokosuka, A., Mimaki, Y., Sashida, Y., 2002b. Spirostanol saponins from the rhizomes of *Tacca chantrieri* and their cytotoxic activity. *Phytochemistry* 61, 73–78.
- Yoshikawa, K., Satou, Y., Tokunaga, Y., Tanaka, M., Arihara, S., Nigam, S.K., 1998. Four acylated triterpenoid saponins from *Albizia procera*. *Journal of Natural Products* 61, 440–445.
- Yoshikawa, K., Katsuta, S., Mizumori, J., Arihara, S., 2000a. Four cycloartane triterpenoids and six related saponins from *Passiflora edulis*. *Journal of Natural Products* 63, 1229–1234.
- Yoshikawa, M., Murakami, T., Oominami, H., Matsuda, H., 2000b. Bioactive saponins and glycosides. XVI. Nortriterpene oligoglycosides with gastroprotective activity from the fresh leaves of *Euptelea polyandra* STEB. et ZUCC (1): structures of eupteleasaponins I, II, III, IV, V, and V acetate. *Chemical and Pharmaceutical Bulletin* 48, 1045–1050.
- Yoshikawa, K., Tanaka, M., Arihara, S., Pal, B.C., Roy, S.K., Matsumura, E., Katayama, S., 2000c. New oleanene triterpenoid saponins from *Madhuca longifolia*. *Journal of Natural Products* 63, 1679–1681.
- Yoshikawa, M., Morikawa, T., Yashiro, K., Murakami, T., Matsuda, H., 2001. Bioactive saponins and glycosides. XIX. Notoginseng (3): immunological adjuvant activity of notoginsenosides and related saponins: structures of notoginsenosides-L, -M, and -N from the roots of *Panax notoginseng* (BURK.) F.H.Chen. *Chemical and Pharmaceutical Bulletin* 49, 1452–1456.
- Yoshikawa, M., Morikawa, T., Nakano, K., Pongpiriyadacha, Y., Murakami, T., Matsuda, H., 2002. Characterization of new sweet triterpene saponins from *Albizia myriophylla*. *Journal of Natural Products* 65, 1638–1642.
- Yoshikawa, M., Morikawa, T., Kashima, Y., Ninomiya, K., Matsuda, H., 2003. Structures of new dammarane-type triterpene saponins from the flower buds of *Panax notoginseng* and hepatoprotective effects of principal ginseng saponins. *Journal of Natural Products* 66, 922–927.
- Yoshiki, Y., Kudou, S., Okubo, K., 1998. Relationship between chemical structures and biological activities of triterpenoid saponins from soybean. *Bioscience, Biotechnology and Biochemistry* 62, 2291–2299.
- Young, M.C.M., Araújo, A.R., Da Silva, C.A., Lopes, M.N., Trevisan, L.M.V., Bolzani, V.D.S., 1998. Triterpenes and saponins from *Rudgea viburnioides*. *Journal of Natural Products* 61, 936–938.
- Yui, S., Ubukata, K., Hodono, K., Kitahara, M., Mimaki, Y., Kuroda, M., Sashida, Y., Yamazaki, M., 2001. Macrophage-oriented cytotoxic activity of novel triterpene saponins extracted from roots of *Securidaca inappendiculata*. *International Immunopharmacology* 1, 1989–2000.
- Yun, T.-K., 2003. Experimental and epidemiological evidence on non-organ specific cancer preventive effect of Korean ginseng and

- identification of active compounds. Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis 523/524, 63–74.
- Yun, Y.S., Shimizu, K., Morita, H., Takeya, K., Itokawa, H., Shiota, O., 1998. Triterpenoid saponin from *Vaccaria segetalis*. Phytochemistry 47, 143–144.
- Zamilpa, A., Tortoriello, J., Navarro, V., Delgado, G., Alvarez, L., 2002. Five new steroidal saponins from *Solanum chrysotrichum* leaves and their antimycotic activity. Journal of Natural Products 65, 1815–1819.
- Zhang, Z., Koike, K., Jia, Z., Nikaido, T., Guo, D., Zheng, J., 1999a. New saponins from the seeds of *Aesculus chinensis*. Chemical and Pharmaceutical Bulletin 47, 1515–1520.
- Zhang, Z., Koike, K., Jia, Z., Nikaido, T., Guo, D., Zheng, J., 1999b. Four new triterpenoidal saponins acylated with one monoterpenic acid from *Gleditsia sinensis*. Journal of Natural Products 62, 740–745.
- Zhang, Z., Koike, K., Jia, Z., Nikaido, T., Guo, D., Zheng, J., 1999c. Gleditsiosides N–Q, new triterpoid saponins from *Gleditsia sinensis*. Journal of Natural Products 62, 877–881.
- Zhang, Z., Koike, K., Jia, Z., Nikaido, T., Guo, D., Zheng, J., 1999d. Triterpenoidal saponins from *Gleditsia sinensis*. Phytochemistry 52, 715–722.
- Zhao, J., Yang, X.-W., Hattori, M., 2001. Three new triterpene saponins from the seeds of *Aesculus chinensis*. Chemical and Pharmaceutical Bulletin 49, 626–628.
- Zhong, H.M., Chen, C.X., Tian, X., Chui, Y.X., Chen, Y.Z., 2001. Triterpenoid saponins from *Clematis tangutica*. Planta Medica 67, 484–488.
- Zhu, N., Jiang, Y., Wang, M., Ho, C.-T., 2001. Cycloartane triterpene saponins from the roots of *Cimicifuga foetida*. Journal of Natural Products 64, 627–629.
- Zhu, N., Sheng, S., Sang, S., Jhoo, J.-W., Bai, N., Karwe, M.V., Rosen, R.T., Ho, C.-T., 2002. Triterpene saponins from debittered quinoa (*Chenopodium quinoa*) seeds. Journal of Agricultural and Food Chemistry 50, 865–867.
- Zou, K., Zhao, Y., Tu, G., Cui, J., Jia, Z., Zhang, R., 2000. Two diastereomeric saponins with cytotoxic activity from *Albizia julibrissin*. Carbohydrate Research 324, 182–188.
- Zou, Z.-M., Yu, D.-Q., Cong, P.-Z., 2001. A steroidal saponin from the seeds of *Allium tuberosum*. Phytochemistry 57, 1219–1222.
- Zou, K., Zhu, S., Meselhy, M.R., Tohda, C., Cai, S., Komatsu, K., 2002a. Dammarane-type saponins from *Panax japonicus* and their neurite outgrowth activity in SK-N-SH cells. Journal of Natural Products 65, 1288–1292.
- Zou, K., Zhu, S., Tohda, C., Cai, S., Komatsu, K., 2002b. Dammarane-type triterpene saponins from *Panax japonicus*. Journal of Natural Products 65, 346–351.